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Original Communications

STUDIES ON THE NUCLEATED RED CELL COUNT IN THE CHORIONIC CAPILLARIES AND THE CORD BLOOD OF VARIOUS AGES OF PREGNANCY

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EVER since the presence of nucleated red cells in the peripheric blood of the newborn infant became known, their significance has been a matter of dispute. In recent years there has been pronounced resumption of this debate. The studies of erythroblastosis naturally have turned to the blood picture in the newborn infant in an attempt to define variations of the normal count.

REVIEW OF LITERATURE

The first investigations as to the presence of nucleated red cells in the blood of the newborn infant are accredited to Neumann[1] in 1871. Lippman,[2] in his study of the newborn blood, listed the observations of several investigators, on the number of nucleated erythrocytes, which we have included in Table I. According to Lippman, Fischel[3] was not impressed by the number of erythroblasts in the normal full-term newborn infant, but he had noticed their presence in premature infants. Loos,[4] Geissler and Japha,[5] in 1895, concluded that normoblasts did not occur in the blood of the normal newborn infant, and that their presence, therefore, must be considered as a pathologic sign. According to Heimann,[6] erythroblasts were not common in icterus neonatorum. Karnitzki[7] found nucleated erythrocytes in the blood of an otherwise normal nursling seven and one-half months of age. In recent years observations were directed to the study of nucleated red cells in erythroblastosis. Buchan and Comrie[8] first noted in 1909 that widespread hemopoiesis is the underlying pathologic condition in icterus gravis. Rautmann[9] and Schridde[10] investigated

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TABLE I. CHRONOLOGIC DATA OF VARIOUS AUTHORS ON NUCLEATED RED BLOOD CELLS

AUTHOR	YEAR	OBSERVATIONS
Neumann, E.[1]	1871	First observer to see nucleated red blood cells in newborn blood.
Vierordt, K.[25]	1872	Confirmed Neumann's observations.
Elder and Hutchinson[26]	1895	Found an average of 5 to 12 erythroblasts per 100 leucocytes.
Carstanjen, M.[27]	1900	Found an average of 1.3 nucleated red blood cells per 100 leucocytes.
Aiken, J.[28]	1902	Found erythroblasts in all cases directly after birth: at 48 hours after birth in 24 out of 25 cases; at 5 to 9 days, 15 out of 27 cases.
Fehrsen, A. O.[29]	1903	Always found erythroblasts present in first two hours after birth; never after thirteen hours.
Takasu, K.[30]	1904	Found nucleated red blood cells in all cases.
Grawitz, E.[31]	1906	Found nucleated red blood cells in 3 of 15 infants.
Biffi and Galli[32]	1908	Observed nucleated red blood cells in 28 of 29 cases.
König, H.[33]	1910	Found nucleated red blood cells in 92 per cent of cases.
Slawik, E.[34]	1920	Found average of 6 nucleated red blood cells per 100 leucocytes present in 14 of 25 cases in second week.
Lučas, W. P., et al.[35]	1921	Found nucleated red blood cells in 52 per cent of cases on first day, with average of 1 per 100 leucocytes; 5 per cent of cases on second day, with average of ½ a nucleated red blood cell per 100 leucocytes.
Lippman, H. S.[2]	1924	Studied 71 infants: greatest number of nucleated red blood cells at birth, with sudden decrease until fifth day when only 1 cell seen in 30 cases. Highest count 37.8 per cent.
Heath, E.[36]	1926	Found minimum value of 0.3 per cent and maximum of 31.3 per cent. Suggested possibility of pathologic conditions with high counts.
Büngeler and Schwartz[12]	1927	Found 1-1.5 nucleated red cells per 100 leucocytes, with highest value 24 per 100 leucocytes. Postulated "birth crisis."
Forkner, C. E.[37]	1929	38.5 per cent of cases had nucleated red blood cells on first day of life.
Javert, C. T.[13]	1939	Found average of 10 nucleated red blood cells per 100 leucocytes.

the pathologic basis of universal edema of the newborn infant. The term "erythroblastosis" was introduced by Rautmann.[9] Kleinschmidt[11] found the blood picture in a case of icterus neonatorum resembled that of an embryo between three and five months of age. We have listed in Table II abnormal values of blood smears in the newborn blood according to various authors. Here we shall call attention to the paper of Büngeler and Schwartz[12] which, unfortunately, did not receive any comment in the literature of recent date. Büngeler and Schwartz,[12] in 1929, did not find any basic differences in the blood pictures which could be correlated directly with the birth weight of premature infants, although the highest number of normoblasts was found in premature infants with very low weights. They also noticed the rapid disappearance of nucleated red blood cells on the second, third, or fourth day of life. This fact has been stressed by Javert.[13] They felt that the nucleated cell count could be used as an indicator of the viability of the newborn infant. According to Büngeler and Schwartz,[12] normoblasts in the blood of the newborn full-term infant are not a physiologic phenomenon in the strict sense but rather conditioned

TABLE II. ABNORMAL VALUES OF NUCLEATED RED BLOOD CELLS
Review of Several Authors

AUTHOR	YEAR	NUCLEATED RED CELLS PER 100 LEUCOCYTES	DISEASE
Schridde, H.[10]	1910	53 nucleated red blood cells per 100 leucocytes	Congenital hydrops
Salomonsen, L.[38]	1931	49 nucleated red blood cells per 100 leucocytes	Congenital hydrops
Shapiro and Cohen[39]	1939	Found values of 369 and 364 nucleated red blood cells per 100 leucocytes	Congenital hydrops
Javert, C. T.[13]	1939	a. Found values of 362, 110, and 1,324 nucleated red blood cells per 100 leucocytes.	Erythroblastosis fetalis
		b. Values of 44 to 52 and 70 nucleated red blood cells per 100 leucocytes.	Congenital abnormalities
		c. Values varying from 20 to 84 nucleated red blood cells per 100 leucocytes.	Prematurity
Wolf and Neigus[40]	1940	a. Found variations from 21, 16, 41, 58, 143, 85 to 300 nucleated red blood cells per 100 leucocytes.	Icterus gravis
		b. Values of 78 and 149 per 100 leucocytes.	Erythroblastosis

by an abnormal act of delivery. Büngeler and Schwartz[12] also noted immature white cells parallel to an increase of nucleated red cells in the first days of life. Conversely, in the absence of immature white cells, nucleated red cells were not present or only in very small numbers. These authors interpreted these cells as signs of, or reactive phenomena to, tissue damage, especially hemorrhages, during the act of delivery. Disintegration of tissue and blood, which is avidly resorbed in this early period of life, leads to a noticeable increase of white cells and, especially, to the liberation of nucleated red blood cells. Injection of embryonic juice into rabbits produced an analogous increase in the number of immature white and nucleated red blood cells. These abnormal cells disappeared from within twenty-four to forty-eight hours. Their elaborate study led them to postulate a "birth crisis" in the blood picture of the newborn infant which they feel is conditioned by tissue damages during the course of delivery. Some data published by these authors seemed of particular significance. In many cases the blood pictures were absolutely identical with those of a normal adult, in spite of the decidedly premature state of the newborn infant. On the other hand, in full-term infants (determined by the usual standards of weight, length, and duration of pregnancy), a considerable increase of immature red and white cells was seen; especially in children born after prolonged labor or after considerable damage to the cranium or other organ systems, as proved by post-mortem examinations.

Among more recent observations, we wish to call attention to those of C. T. Javert[13] who believes that routine cord blood smears can be used as a more accurate criterion of prematurity and maturity than the standards so far accepted. This statement certainly cannot be reconciled with the studies of Büngeler and Schwartz.[12] According to Javert,[13] a certain number of nucleated red cells (10 or more) per 100 white cells, is in itself a sign of prematurity, regardless of whether or not weight, length, and duration of pregnancy are also pointing to prematurity. That high nucleated red cell counts might be caused by asphyctic conditions, as for example, in congenital heart disease, is pointed out in the paper by Hellman and

Hertig.[14] They found such an increase of nucleated red cells which, in examining the chorionic capillaries, might be confused with erythroblastosis. Javert,[13] too, has noted that in the blood smears from cases with different abnormalities and from asphyxiated babies, in general, an increased number of nucleated erythrocytes was found.

It is the purpose of this paper to add more material to this question, dealing with the number of nucleated red cells in the newborn infant, which is still unsettled, as we believe. Correlation of post-mortem findings to the blood picture seen in the cord smears seems of distinct value, especially with regard to some of the views expressed in the recent literature. At the same time we also wish to add in the frame of this study more material of simple diagnostic value in the very early phases of pregnancy, as revealed in routine examinations of curettings from abortions. Ever since 1930 this histologic procedure, introduced by K. Terplan, has proved its reliability in determining the age of pregnancy, especially in the first twelve weeks. Ryerson and Sanes[15] have summarized the entire material examined in the Pathological Laboratory of the Buffalo General Hospital until the year 1934. While in our routine histologic procedures the number of nucleated red cells in chorionic capillaries was more or less roughly estimated, Ryerson and Sanes[15] actually enumerated the nucleated red cells and determined their ratio to the nonnucleated red cells in the chorionic capillaries. With this ratio the age of the pregnancy within the early phases could be determined fairly accurately, and these estimates in many cases could be controlled by reliable clinical data and the length of the embryo. The figures reported by Ryerson and Sanes[15] were confirmed by Ohringer,[16] in Germany, and by Halpert and Stasney,[17] in this country. Ryerson and Sanes[15] mentioned the possibility that counting of nucleated red cells in the chorionic capillaries might be used to detect fetal erythroblastosis in more mature pregnancies.

We wish to show that examination of the nucleated red blood cells in the chorionic capillaries reveals rather constant figures for the normal newborn infant. Whenever these values are altered, certain conclusions may be drawn.

MATERIAL EXAMINED

Two hundred and sixty placentas were received, as a rule immediately following delivery. These included full-term and premature births and also some late abortions. There were 200 placentas at full term. They were weighed, diameters measured, carefully inspected, and any findings of infarcts, length, and insertion of cord recorded. Sections in vertical and horizontal (parallel) planes were taken and for forty-eight hours fixed in Orth's fluid (this mixture was given preference because of its excellent fixation of the red blood cells). They were embedded in paraffin in the usual way. Sections were cut at 8 microns and stained with hematoxylin-eosin. One thousand red blood cells were counted within the lumina of the chorionic capillaries with the oil immersion lens. The ratio of the nucleated to nonnucleated erythrocytes, as found in the placentas, is given in Fig. 1.

In addition to this enumeration of red blood cells in the chorionic capillaries, blood was aspirated from the umbilical cord of full-term and premature infants, including also all those cases of abortions in which blood could be obtained. The smears were

stained according to Wright's method. The usual differential count of 100 leucocytes was done, and as nucleated red blood cells (normoblasts, erythroblasts, proerythroblasts) appeared, they were counted separately. That number, therefore, is related to 100 white cells. Our findings are recorded in Fig. 2.

In many instances of fetuses under 2,500 Gm., we were unable to correlate the cord blood smear with the findings in the chorionic capillaries. In some of these, we had received only the placenta, and cord blood smears were not obtainable. In addition, we were fortunate to have the opportunity to study cord blood smears from 4 cases of erythroblastosis and the placenta in one of these.

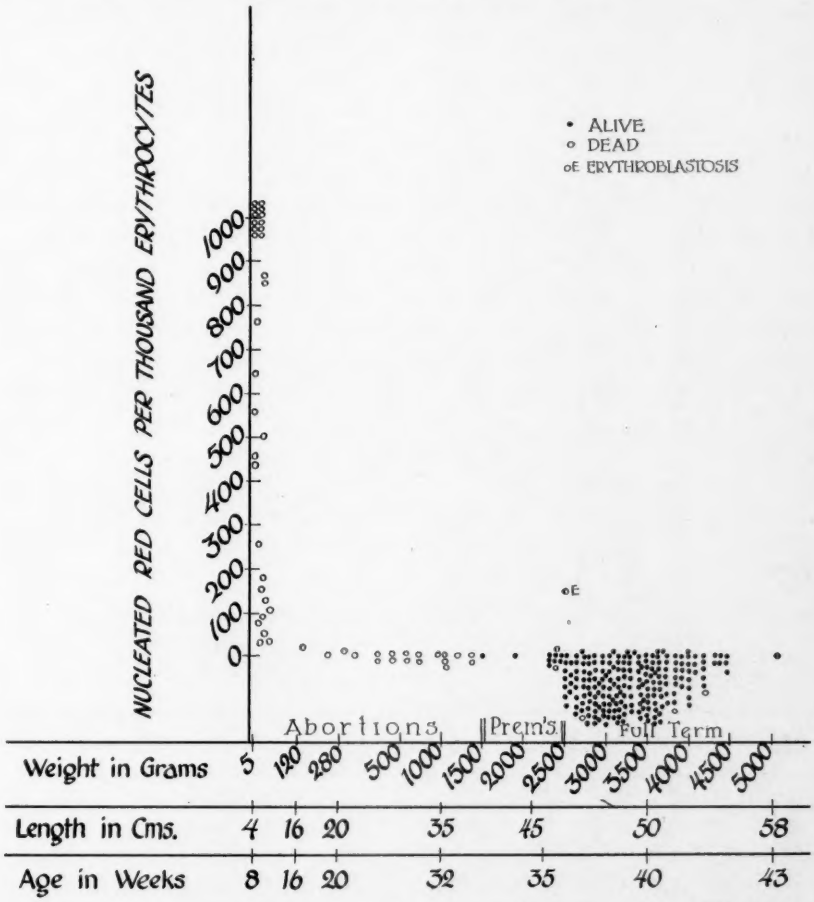

Fig. 1.—Scattergram, showing nucleated red cell counts per one thousand erythrocytes in the chorionic capillaries of 260 placentas examined in various ages of pregnancy, correlated with the weight in grams, length in centimeters, and the age in weeks.

RESULTS

a. *Full-Term Infants (Weight Above 2,500 Gm.).*—Of the 260 placentas studied, 200 were in this group. The average weight of the infants was 3,377.6 Gm. and average length was 50.7 cm. Examination of the chorionic capillaries in the placentas of this group revealed absence of nucleated red cells in counting 1,000 erythrocytes in 166 placentas. In 33, one nucleated cell per 1,000 nonnucleated erythrocytes was found. Only in one case which was that of an asphyxia and in which the umbilical cord smear showed more nucleated red cells than are usually seen, we found 3 nucle-

ated cells in the chorionic capillaries per 1,000. The average count of nucleated red cells in the cord blood smears of these 200 infants was 7.3 per 100 leucocytes. This includes the five fatal cases with a much higher count of nucleated red cells in each (see Table III). In the majority of these cases the number of nucleated red cells ranged between zero and ten. Many of these were around 6; in 8 instances the count was above 10, varying between 12 and 24. Variations of weight and length of the infant had apparently no effect on this figure. In the microphotograph (Fig. 3, *A* and *C*), this very rare occurrence of nucleated red blood cells in the chorionic capillaries of a full-term placenta is shown.

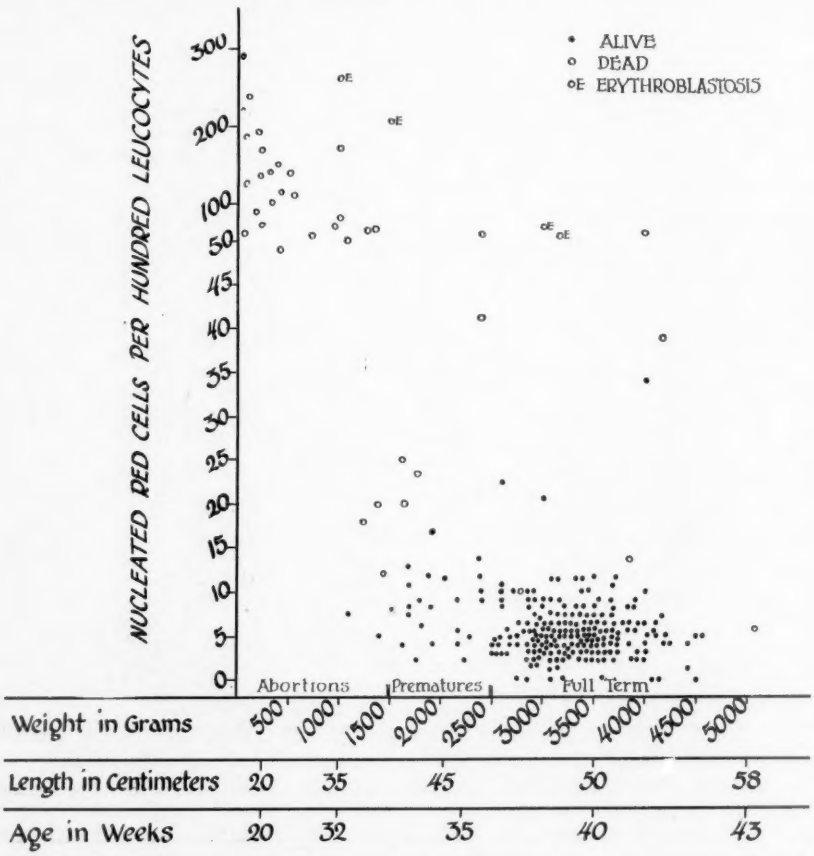

Fig. 2.—Scattergram, showing nucleated red cell counts per one hundred leucocytes in 260 cord blood smears of various ages of pregnancy, correlated with the weight in grams, length in centimeters, and the age in weeks.

b. *Prematures (From 1,500 to 2,500 Gm.).*—In this group, 30 cord smears and 11 placentas were studied. Twenty-five live infants had a nucleated red count of 11 per 100 leucocytes. The remaining 5, all of which died or were stillborn, had an average count of 57.3 per 100 leucocytes (Table III). This makes a total average of 21 nucleated red blood cells per 100 leucocytes. In 6 of the 30 placentas which were examined, the chorionic capillaries showed the presence of one nucleated red cell per 100 erythrocytes. In the other five, 2 per 1,000 erythrocytes were found.

c. *Abortions (under 1,500 Gm.).*—In this group, 49 placentas and 30 cord blood smears were examined. The results are recorded in Figs. 1 and 2. The average count for abortions is 101.7 nucleated red cells per 100 leucocytes. This figure, of

course, includes a wide variation in the age of pregnancy which was terminated by abortion and, as the accompanying graphs illustrate, counts as high as from 200 to 300 nucleated red blood cells per 100 leucocytes were found in the abortion of a twelve weeks' pregnancy. Correspondingly, we found values of 10 nucleated red blood cells per 1,000 erythrocytes in the chorionic capillaries in these cases in which the pregnancy was about three months of age. This value increased rapidly

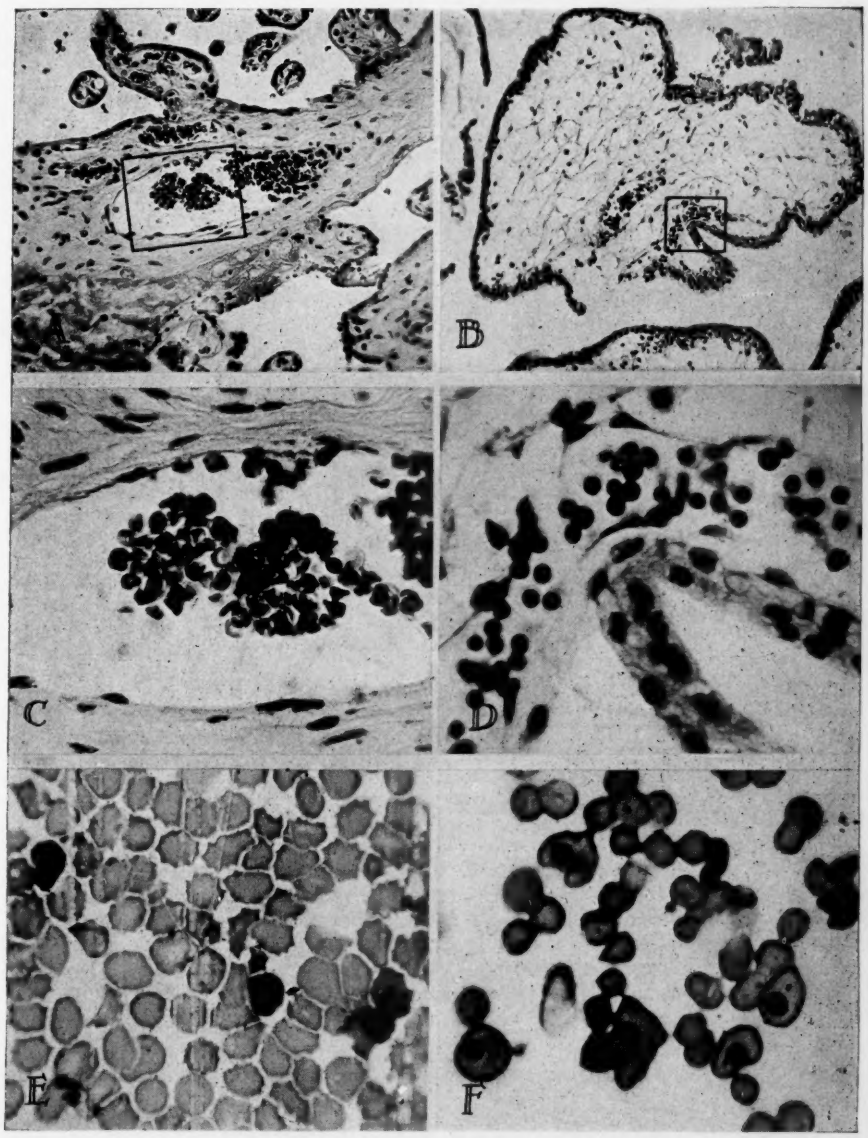

Fig. 3.—(*A*) Section through the placenta, illustrating the chorionic capillary of a full-term infant (low power). (*B*) Section through a chorionic villus of a six to eight weeks' pregnancy, illustrating the nucleated red blood cells in a capillary (low power). (*C*) The chorionic capillary of *A*, showing absence of nucleated red blood cells (oil immersion). (*D*) Chorionic capillary of the ink-marked area in *B*, showing numerous nucleated red blood cells. (*E*) Wright's stain preparation, showing nucleated red blood cells taken from a case of erythroblastosis. (*F*) Wright's stain preparation of nucleated red blood cells from a fetus of three months' gestation.

TABLE III. CAUSES OF DEATH AND NUCLEATED RED BLOOD CELLS PER 100 LEUCOCYTES AND 1,000 ERYTHROCYTES

CASE	NUC. R. B. C. CORD SMEAR	NUC. R. B. C. CHORIONIC CAP.	LENGTH (CM.)	WEIGHT (GM.)	AUTOPSY FINDINGS
			Full-Term Infants		
M. K.	14/100	0/1000	52.0	3820	Intermeningeal and subdural hemorrhages. Tentorial tears. (Stillborn.)
D. S.	10/100	0/1000	55.0	2720	(Craniotomy.) Extensive maceration.
S. B.	38/100	0/1000	52.5	4210	Empyema (died on seventh day). Hemorrhages in kidney and scalp. Hemorrhagic pleuritis.
G. M.	6/100	0/1000	50.0	5280	Cephalematoma (stillborn). Atelectasis of both lungs. Autolytic fetus.
B. G.	54/100	0-1/1000	51.0	2530	Asphyxia (died 1 hour after birth). Diffuse hemorrhages in adrenals and both lateral ventricles.
	23.2/100	>1/1000	51.7	3712	Average
			Premature Infants		
M. L.	72/100	2/1000	42.5	2450	Aspirated mucus in major bronchus. Subperiosteal hematoma and scalp hemorrhage. Atelectasis of both lungs. (Lived 7 hours.)
F. A.	68/100	3/1000	38.0	1620	Fetal atelectasis. (Stillborn.)
L. A.	74/100	2/1000	40.0	1560	Tentorial tears. Intermeningeal and pleural hemorrhages. Atelectasis (lived 2 days).
G. R.	41/100	1/1000	48.1	2480	Intratentorial and intermeningeal hemorrhages. Also hemorrhages in lungs.
A. G.	22/100	0/1000	37.0	1520	Acrania and anencephaly. Encephalocele.
	57.3/100	2/1000	41.2	1926	Average

in the abortions of younger age, until in those very early pregnancies from six to eight weeks' duration, practically all of the red blood cells in the chorionic capillaries were found nucleated (Fig. 3, *B* and *D*). A representative cord smear from a three months' fetus is illustrated in Fig. 3, *F*. However, in this same series of two infants, weighing 1,400 and 1,100 Gm., we found only 7 and 5 nucleated red cells per 100 leucocytes in the cord smear. These infants remained alive.

d. *Twin Infants.*—There were three sets of twins in this series. Their average weight was 2,665 Gm.; their average length 46 cm. Five nucleated red cells per 100 leucocytes were seen in the cord blood smear, and no nucleated red cells were found in the chorionic villi.

e. *Race.*—There are 17 negro infants in this series. Their average weight was 3,153.7 Gm., and their length 49.4 cm. The average nucleated red count per 100 leucocytes was 7. No nucleated red cells were found in the chorionic capillaries.

f. *Mortality.*—The mortality rate is 2.5 per cent for the 200 full-term infants. Post-mortem findings are tabulated in Table III. These findings are not complete, especially in the premature group. In some cases, it took many days until a post-mortem consent could be obtained. In these and in others, an extreme autolysis of

the tissues at the time of autopsy prevented a reliable morphologic analysis. This applies also to the umbilical cords, and cord blood studies could not be made in some of these cases. As seen in Table III, a distinctly increased number of nucleated red cells was found in the cord blood of the dead infants in each group.

g. *Maternal Statistics.*—The average age of the mothers in this series was 25.2 years. Eighty-three of these were primiparas, with an average age of 22.4 years. No variations in the nucleated red blood cell count were observed relative to parity or age of the mother. The average weight of the mothers at the time of delivery was 152.4 pounds; the average weight gained during pregnancy was 25.0 pounds. No difference was observed relative to the weights or the weight gained in infants born of these mothers. The average count of nucleated red cells was 7.1 per 100 leucocytes. In addition, this count was apparently not altered by such complications as mitral stenosis, pre-eclampsia, hypertension, and syphilis. The average erythrocyte count of the mother on the day of admission was 3,895,000 with a hemoglobin of 77.6 per cent. No correlation could be found between the red cell count and hemoglobin of the mother and the nucleated red cell count in the cord smears. Our series includes 4 patients with severe anemia and 1 patient with myelogenous leucemia, all of whom delivered normal babies without alteration of the nucleated red cell count in the cord smears or in the placentas. Stimulated by the studies of Büngeler and Schwartz,[12] we have tried to correlate our blood studies with the length of labor and the method of delivery. As previously noted, variations in the count of primiparas and multiparas, as a group, were negligible. Our findings are listed in Table IV.

TABLE IV. METHOD OF DELIVERY AND AVERAGE NUCLEATED RED COUNTS PER 100 LEUCOCYTES

LENGTH OF LABOR	CASES	SPONTANEOUS	CASES	LOW FORCEPS	CASES	BREECH
Under 10 hours	49	6.9/100	21	5.2/100 leucocytes	2	6/100
10-20 hours	43	6.8/100	25	6.6/100	1	10/100
20-30 hours	18	7.8/100	12	10.3/100	1	6/100
30-40 hours	4	6.0/100	6	9.6/100	0	----
40-50 hours	3	5.0/100	6	9.8/100	0	----
Over 50 hours	1	5.2/100	3	8.1/100	0	----
	118	6.3/100 Average	73	8.3/100 Average	4	7.3/100 Average

The 5 deaths are not included in this analysis. However, we did not feel, in analyzing each of these cases individually, that the increased count of nucleated red cells which was found in each one was conditioned by the type of delivery. Our Table IV shows that there is no marked variation of the nucleated red cell counts dependent upon length of labor or method of delivery.

The average weight of the placentas in the full-term infants was 641.07 Gm. Weight, insertion of cord, infarcts, and length of cord were noted, but no correlation could be established between these findings and the nucleated red blood cell count. The length of the cord played no part except in one case. In this it measured 115 cm. and was found coiled about the baby's neck. It was felt that this finding was the cause of death from severe asphyxia. The number of nucleated red cells in this case was 50 per 100 leucocytes, but only 2 to 3 nucleated red cells were seen among 1,000 erythrocytes in the chorionic capillaries of the placenta of this case.

Erythroblastosis: We have had four cases of erythroblastosis in our series. The cord blood smears gave the following counts of nucleated red cells per 100 leucocytes: 260, 210, 74, and 56. In only one case was it possible to examine the placenta. In this, 142 nucleated red cells could be counted per 1,000 erythrocytes within the chorionic capillaries. Fig. 3*E* shows the typical findings in one of these cases with universal edema. In this case, the stillborn infant was already considerably autolytic. An exact morphologic analysis of the blood smear was impossible, but the nucleated red cells within the capillaries of the placenta could be readily enumerated.

DISCUSSION

The conclusions of Ryerson and Sanes[15] as to the number of nucleated red cells in the chorionic capillaries were based on the ratio between nucleated red cells and erythrocytes. They were of especial importance in determining the early phases of pregnancy from four to twelve weeks' duration, and comparing such figures to all those obtained from placental tissue in pregnancies older than twelve weeks. For this determination it was entirely sufficient to enumerate 100 erythrocytes. In amplifying their studies, we have demonstrated that in late abortions, but especially in the placentas of premature and mature pregnancies, it is necessary to count at least 1,000 erythrocytes in order to find one or, in a few cases, more nucleated red blood cells. Obviously, the cord smear gives us a more easily accessible means of determining the relative number of nucleated red cells. The erythroblast-leucocyte ratio might be found distinctly increased in premature infants in certain malformations and in all infants with very severe asphyxia, but this increase of nucleated red cells is not as striking in the ratio of erythroblasts to erythrocytes in a histologic analysis of the chorionic capillaries. This, as Ryerson and Sanes[15] already have pointed out, might be of considerable diagnostic value, especially in cases of erythroblastosis. In one of our cases of erythroblastosis, 142 nucleated red cells were numerated per 1,000 erythrocytes. On the other hand, in cases of asphyxia, this ratio never exceeded 2 to 3 per 1,000 erythrocytes.

It has been stated already by Büngeler and Schwartz[12] that the value of routine hematologic examination, including cord smears, at the time of delivery, and especially applied to premature babies, lies in prognosis. Javert believes that a low count of nucleated red cells in full-term infants is indicative of a more mature hemopoietic system. Conversely, premature infants, on the basis of weight and length, may have an immature hematopoietic system.

One-third of the premature cases in Group II in Javert's paper shows entirely normal counts. In addition, in 20 per cent of the mature Group I no nucleated red cells were seen at all. In 32 per cent of the same group, consisting of babies of normal or even excessive size, the blood smear gave the "premature" picture. In several cases of Group II in which a post-mortem examination was performed, distinct pathologic changes, especially subarachnoid hemorrhages, were found.

In our own very limited post-mortem series, in all full-term infants, severe hemorrhages, caput succedaneum or cephalematoma were found. In two instances with nucleated red cell counts of 6 and 10, respectively, death had occurred apparently previous to delivery. There were extensive maceration and considerable hemolytic fluid in the pleural cavities. Craniotomy had to be resorted to in one, while in the other, in spite of severe maceration, small suffusions were seen in the scalp. In our premature group, in all cases exceeding the weight of 1,000 Gm., distinct evidence of birth injury was present: suggillation in the scalp, subperiosteal hematoma, tentorial hemorrhages, multiple petechial hemor-

rhages in the serous membranes, hemorrhages in the lung parenchyma, and, in one case, very severe malformation with a huge encephalocele and extensive rachischisis.

From our series, as well as from the findings of Javert,[13] and especially from those of Büngeler and Schwartz,[12] it seems evident that nucleated red blood cells are frequently absent. This applies not only to mature infants but, within certain limits, also to prematures. What the actual or best controlled number of nucleated red cells in the large normal material from entirely normal deliveries really is, we hesitate to state with too rigid figures. In all probability, slight variations between zero and 5 to 10 will continue to be found, in line with the biologic differences of individuals and of such individually conditioned events as the birth of a child. We are inclined to agree with Büngeler and Schwartz[12] as to the ever ready responsive ability of the normal bone marrow to tissue damage, with or without asphyxia. Certainly asphyxia seems to play an important causative role in this entire complex, in many cases. What all these figures really reflect is the state of the bone marrow at the time of or immediately following delivery; but we do not know whether the state of the bone marrow preceding the time of delivery is also reflected by these figures. It might be in the normal fetus close to, if not identical with, the count in a normal infant. If the bone marrow does react in some instances with liberation of an abnormal number of embryonic forms of red and white cells into the circulating blood, then we might remember that this is the very nature of any normal bone marrow, not only at the time of birth but occasionally also in adult life in reaction to some severe injury as, for instance, extensive hemorrhagic infarctions or other inner hemorrhages. It is the very nature of the bone marrow that it is always in an embryonic state. Such reactions are in line with the experience of Büngeler and Schwartz[12] who found this sometimes more pronounced in the premature group and especially in infants below 40 cm. in length and 1,000 Gm. of weight. If within one to three days these reactive forms disappear completely, we could hardly consider this fleeting phenomenon an expression of a premature state of the bone marrow. In every other respect, however, our figures seem to confirm the findings of Javert,[13] especially in regard to the average count of nucleated red blood cells found in the smears from the umbilical cords.

Some of the differences in the numbers of nucleated red cells, as encountered in the literature, might be due to mere technical features. Büngeler and Schwartz[12] and Javert[13] have called attention to the higher count of nucleated red cells in the cord blood and the quick drop of nucleated forms in the smear taken from the blood of the newborn infant within the first twelve to twenty-four hours, leading to their complete elimination within a very few days.

Quite reluctantly, we have added our own results to this problem of number and significance of nucleated red blood cells in the newborn infant at the time of delivery. Our material is admittedly small. Small also is the number of post-mortem examinations which could be used for this study, but notwithstanding this deficiency, we feel these find-

ings should be reported, as their correlation to the hematologic findings from the cord blood appears of some value. We wish to urge more complete recording and reporting of normal or pathologic findings in the newborn infant, but more so in the stillborn, especially in such instances in which an abnormally high nucleated red blood cell count was seen in the cord smear and, reversely, also in those cases in which this count was not increased, as these might prove just as important. In addition, all such cases seem to be of great interest in which an unusually high number of nucleated red cells is encountered in the blood smear in an otherwise normally appearing infant. This blood smear might have a frank erythroblastosis-like appearance and still the anticipated change for the worse does not take place. Within a few days, the count returns to normal. We had such an experience recently.

A primipara was delivered of a full-term baby boy of 4,240 Gm. in weight and 53 cm. in length. The number of nucleated red cells on the day of delivery was 950 per 100 leucocytes, on the third day 104 per 100 leucocytes, and on the fifth day 55 per 100 leucocytes. The most interesting feature regarding this unusually high number of nucleated red cells is the fact that the labor had lasted for over seventy-four hours. But, as far as we know, the baby's subsequent development was normal.

Whether or not we should consider this recent experience of ours as exceptional, we believe as before in the great value of the cord blood smear in detecting cases of erythroblastosis.

Wintrobe and Schumaker[18] have compared the blood picture of patients with pernicious anemia during the response to liver therapy with the blood of the fetus. Liver extract has been used experimentally (Wintrobe[19] on this basis in rabbits), but it failed to bring about an increase in the blood values. Wigodsky and Ivy[20] working with rats, Bruner,[21] and Reimer,[22] who repeated these experiments with chick embryos, also failed in detecting any changes in the blood formation of the embryo. Recently Jones[23] has observed changes in the primitive blood formation of an eleven-day rat embryo, following parenteral administration of liver extract to the mother. He repeated these experiments with diets containing desiccated hog's stomach, and this also influenced embroyonic erythropoiesis. Schlicke[24] fed pregnant albino rats with human gastric juice. This produced a significant increase in the number of nucleated erythrocytes, but it had no effect on the relative number of reticulated or nucleated red blood cells of the newborn.

We believe that the answer to these problems might have a direct bearing on a better understanding of several blood dyscrasias, not only of the newborn infant but of the adult as well. The experimental study of the nucleated red cell in embryonic life may prove a useful adjunct in the development of therapeutic agents in the future.

CONCLUSIONS

1. Systematic histologic study of the chorionic capillaries of placentas of various ages gave the following results as to the relative number of nucleated red cells:

a. In early pregnancies (up to the sixth and seventh week), practically all of the red blood cells are nucleated.

b. By the twelfth week, values of 10 or less nucleated red blood cells per 1,000 erythrocytes were counted.

c. In full-term pregnancies, one or two nucleated red blood cells per 1,000 erythrocytes were found in the chorionic capillaries of the placentas in 16.5 per cent of our series. In the remaining 83.5 per cent, no nucleated red cells were seen, counting 1,000 erythrocytes.

2. The results of our hematologic cord blood smears relative to the ratios of nucleated red blood cells to 100 white cells were as follows:

a. In early and late abortions, variations between 10 and 300 per 100 leucocytes, with an average of 101.7 nucleated red blood cells per 100 leucocytes, were found.

b. In premature infants, 21 nucleated red cells per 100 leucocytes were observed.

c. In full-term babies, 7.3 per 100 leucocytes were found.

3. Age, weight, weight gain, parity, blood pressure level, complications of pregnancy, including anemias, did not seem to affect this ratio.

4. Variations of weight and length of the fetus within the two groups of premature and mature babies did not influence the ratio.

5. In twins the average count was distinctly lowered.

6. In stillbirths and babies which died within the first ten days of life a higher nucleated red cell count was observed.

7. In babies with congenital abnormalities, and especially in severely dyspneic babies, higher nucleated red cell counts were found.

8. The nucleated red blood cell-leucocyte ratio was considerably altered in many babies in this series, but this was not so with the nucleated red blood cell-erythrocyte ratio in the same babies; however, in all cases of erythroblastosis, the marked increase of nucleated red blood cells was reflected in both ratios.

9. Cord blood smears and examination of chorionic capillaries are most useful in detecting cases of erythroblastosis.

10. A decided increase of nucleated red cells, in our opinion, points to pathologic states or events in the newborn infant, occurring during the course of delivery (the "birth crisis" of Büngeler and Schwartz[12]). This applies especially to asphyxia and its associated hemorrhages (birth injury in the broadest sense).

11. The cord blood smear is of decided prognostic value as to life, especially in the premature infant.

12. Nucleated red counts closely approaching or identical with that of the normal adult should be considered as the ideal physiologic blood count of the newborn infant. We feel that such a count is consistent with a normal, easy delivery, a normal state of the bone marrow in the premature as well as the full-term infants, with absence of any birth injury.

I am deeply indebted for the untiring effort and sincere interest of Drs. Kornel Terplan and F. C. Goldsborough, under whose direction this study was attempted. In addition, the splendid cooperation of Mrs. Alice Busch and Mr. Melford Diedrick in the preparation of data and photomicrographs, and the aid and suggestions of the many interns, nurses and students of the Department of Obstetrics of the Buffalo General Hospital, have been invaluable and sincerely appreciated.

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INTRAUTERINE RESPIRATION IN RELATION TO DEVELOPMENT OF THE FETAL LUNG

With Report of Two Unusual Anomalies of the Respiratory System

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ANIMAL experiments carried on by several investigators during the past few years have shown beyond doubt that respiratory activity on the part of the fetus can occur in utero. One group believes that this activity is always present and that it plays an active part in the normal development of the pulmonary alveoli. Another group believes that respiratory activity is not physiologic and does not occur unless abnormal conditions exist.

This paper briefly reviews the work leading to these contradictory conclusions, presents a brief description of alveolar development and subsequent alveolar expansion, and reports two congenital anomalies which indicate that the inflow and outflow of amniotic fluid is not essential for normal alveolar development.

SUMMARY OF LITERATURE

Snyder and Rosenfeld,[1] working with rabbits and other animals, and Barcroft and Barron,[2] using sheep, have definitely shown that, with the conditions under which they worked, movements of the chest wall similar to those normally asso-

ciated with respiration occur before birth. These movements are visible through the uterine wall but are better observed when the abdomen is opened in a saline solution at body temperature and the fetuses are delivered into the bath, the placental circulation being kept intact. If India ink is added to the water bath, the ink may be demonstrated in the alveoli of the fetuses that have exhibited respiratory movements,[3] definitely indicating that the rhythmic respiratory movements can result in an exchange of amniotic fluid between the alveoli of the unborn animal and the amniotic cavity.

These respiratory movements commence early in pregnancy, and Snyder and Rosenfeld[4] believe that in addition to being a normal function of the fetus they play a major role in the development of the lungs. The statement is made that any impediment to the inflow of amniotic fluid will affect the development of the alveoli, resulting in atelectasis. According to the authors, "Fetal respiration aids in the structural differentiation of the normal lung. The normal development of the alveoli may be complicated by the presence of amniotic fluid containing debris of excessive amount or abnormal type. A mechanical obstruction of bronchioles brought about during embryonic life may interfere with the normal flow into the lung of amniotic fluid and result in incomplete dilatation of alveoli; i.e., atelectasis."[4] Also, "There is evidence that intrauterine respiration is of functional significance in the development of a normal lung, aiding in dilatation in alveoli and elastic walls of the future air passages."[3]

Windle and his co-workers,[5, 6] on the other hand, insist that any operative procedure involving the uterine wall immediately initiates abnormal changes in the fetal environment and that these changes interfere with the normal maternal-fetal oxygen exchange, so that the action of the fetus under such circumstances cannot be considered normal. He believes that although respiratory movements of the chest can occur, they are not found under normal conditions and do not always result in aspiration of amniotic fluid into the alveoli. His conclusions are based on experiments in which he injected thorotrast into the amniotic cavity of unanesthetized, unoperated guinea pigs and then observed them with periodic x-rays. The thorotrast could be demonstrated in the fetal lungs only when abnormal conditions such as anoxemia or dystocia existed.

The fact that the fetuses observed by Snyder and Rosenfeld breathed normally and survived after they were removed from the water bath and the cord severed, and that various animals exhibited a uniform response while in the bath to changes in oxygen, carbon dioxide or drug content of the maternal blood, indicate that these authors must be fairly correct in their assumption that the environment of the animals is not greatly altered by the operative procedures.

To what extent these animal experiments may be considered indicative of similar activity on the part of the human fetal lung has not yet been proved. By carefully observing the abdomen of a pregnant woman, rhythmic movements can occasionally be seen[7, 8] which are independent of maternal movements and are believed due to fetal breathing. A few attempts have been made to identify radio-opaque material in the human fetal lung following its introduction into the amniotic fluid of pregnant women. Reifferscheid and Schmeimann[9] injected ambrothor into the amniotic fluid of women whose pregnancies were about to be interrupted. By fluoroscopy before operation and by microscopic examination after death, they demonstrated the substance in the fetal lungs. They described it as moving rhythmically back and forth in the bronchial tree and stated that they could demonstrate it as early as the fourth or fifth month of pregnancy.

Windle,[5] however, mentions 6 cases studied in a similar manner by Dr. Cornell in which diotrast, injected into the amniotic cavity, could not be demonstrated in the fetal lungs. Bufe[11] delivered one of a pair of human twins at six months' gestation into a water bath at cesarean section and was unable to elicit respiratory movements until the oxygen content of the fetal blood was diminished. He states that by taking roentgenograms of other fetuses in utero at few second intervals over periods of several hours he was able to convince himself that movements of the thoracic cage did not occur.

It should be noted that the technical difficulties involved in studying the human fetus are great, and one must be very cautious in drawing definite conclusions relative to the respiratory activity of the human fetus at the present time.

Microscopic examination of the lungs of stillborn fetuses and infants dying a few hours or days after birth frequently reveals the presence of squamous epithelial cells desquamated from the fetal skin, vernix caseosa and material from the fetal intestinal tract in the alveoli. These substances cannot be demonstrated in all cases and this fact has led to the belief that their presence is abnormal. They have most generally been considered a result of stimulation of the respiratory center by decreased oxygenation of the blood while the fetus was still in utero, and have been considered a sufficient basis for the diagnosis of intrauterine asphyxia.[11, 12] Those who believe this material is constantly present in the alveoli explain its apparent absence as being due to marked dilution which may result from an increase of amniotic fluid, from decreased amounts of solid particles in the fluid, or from both. They also believe that its distribution in the lungs may be patchy and that if a sufficient number of sections are examined the amniotic elements almost invariably can be seen. If this conception is true, the old idea that amniotic fluid in the lung is an indication of asphyxia must be abandoned, and the fluid must be considered a normal physiologic constituent. In any event, the presence of amniotic elements is definite evidence that amniotic fluid can enter the human fetal lung and that it probably does so as a result of active inspiratory movements.

LUNG DEVELOPMENT

The alveoli in the fetal lungs develop as solid masses of cells which grow, become canalized, and subsequently resemble small hollow balls lined by large cuboidal cells. Increase in alveolar caliber is due, in early fetal development, to multiplication of these cuboidal cells, but later it is brought about largely by the invasion of capillaries derived from the underlying blood vessels into this originally continuous lining.[12] The capillaries force their way inward between the cells, so that at term the alveolar lining is composed of naked capillaries with the original cuboidal cells persisting only in the small spaces between them. The alveolar walls are thus greatly increased in surface area and are given a uniformly irregular appearance somewhat similar to that of partially crumpled paper sacks (see Fig. 4).

With the expansion which follows initiation of respiration after birth, the slack is gradually taken up, the alveolar walls become much less irregular in pattern, and the alveolar volume is greatly increased. The change from an unexpanded to an expanded state is a gradual process that requires several days for completion.

The lung which has never contained air is generally described as being atelectatic, but when used in this connection, the term is misleading. It is usually used to indicate collapse of alveoli with obliteration of all lumina, and in this sense is not true of the fetal lung. The alveoli become larger and modified in shape with progressive intrauterine development, but the walls are never collapsed and after the first few months a lumen is normally present in each alveolus. Since a lumen is present, something must fill the space; it cannot be air and it must, therefore, be fluid. Two sources are possible: aspiration of the media in which the fetus is immersed or transudation of body fluid through the alveolar walls. As mentioned previously, Snyder and Rosenfeld believe it is the former and that it is necessary for normal development. Evidence derived from a study of the malformations to be described shows that it can be the latter and that normal lung development may occur without the inflow of amniotic fluid.

DISCUSSION

A well-known pathologic state exists in the hypoplasia of lung tissue which is associated with failure in development of the diaphragm and herniation of the abdominal viscera into the thoracic cavity. Both lungs are almost always smaller than normal but the greatest reduction in size occurs in the one on the same side as the diaphragmatic defect. The histologic structure of these lungs is most interesting. Instead of exhibiting alveoli histologically normal for the period of gestation at which the fetus is delivered, the lungs manifest a state of immaturity comparable to that found in a more immature fetus whose lungs normally would be of such size and weight. The small size is not due to collapse of alveoli; instead, cuboidal epithelial cells form a proportionately greater part of the alveolar walls and capillary ingrowth has been arrested so that alveolar development is incomplete. The degree of hypoplasia exhibited histologically is comparable to the degree of immaturity visible grossly.

Lungs even more hypoplastic may be found occasionally in association with massive pleural effusions. In one case, a fetus 45 cm. in length recently observed at the Chicago Lying-in Hospital, the combined weight of the lungs was 3.6 Gm. (average for a fetus of this size is 44.2 Gm.). We have seen several other cases with similar but somewhat less marked hypoplasia from the same cause. In all of these cases the pleural effusion must have developed in the first few months of fetal life in order to have arrested lung development at such an early stage. The histologic immaturity of these lungs, as well as that associated with diaphragmatic hernias, is approximately equivalent to that found in lungs of equivalent size in normally developed premature fetuses.

The immaturity of the lungs associated with diaphragmatic defects or pleural effusion might be due to a direct inhibition of growth caused by lack of space for development, or it might be secondary to a lack of space for the inflow and outflow of amniotic fluid. This question cannot be answered from these cases.

We have recently observed two different anomalies which add materially to our knowledge. The first was observed on our own service and the second was very kindly sent to us by Dr. Aaron Gunther who performed the autopsy.

In the first of these (Fig. 1), a mass of lung tissue was found in the left pleural cavity which had no connection with the trachea and into which, therefore, amniotic fluid could not enter. It was present in an infant with an associated left-sided diaphragmatic hernia, and the three divisions of lung tissue (right, left, and accessory lungs) showed an extremely interesting histologic pattern which is described in the autopsy protocol at the end of the paper. The unconnected mass of lung tissue (Fig. 2) and the right lung are composed of alveoli similar to the expected appearance in an infant at term, while those in the left lung are modified by the existence of the diaphragmatic hernia. Why the accessory lung should not have been more greatly compressed and more inhibited in its development is difficult to understand. It may possibly have been protected from direct compression by its location in a pocket

behind the heart. At any rate, although it was entirely impossible for amniotic fluid to have entered the alveoli, the alveolar spaces were large and the walls normally developed.

In the second infant (Fig. 3) tracheal obstruction resulted from a malformation of the cricoid cartilage. The obstruction was complete except for a minute canal approximately 1 mm. in circumference located behind the cartilaginous mass which produced the occlusion. It formed the only connection between the larynx above and the trachea below. The lungs were large, well developed and entirely normal histologically (Fig. 4). Although there was a connection between the larynx and the trachea it was by a canal so small that its identity could be definitely established only with the aid of a dissecting microscope. One cannot deny the possibility that amniotic fluid in the pharynx might have leaked into the trachea and thence into the lungs, but it is inconceivable that such a minute opening would permit an inflow and outflow of amniotic fluid at a rate comparable to that at which intrauterine respiration is believed to take place. No debris which might have been derived from amniotic fluid was present in the alveoli of any of the sections studied.

Thus, in these two cases, normal alveolar development occurred despite the fact that in the first instance the alveoli had no connection whatever with the amniotic cavity and that in the second case there was a definite and marked impediment to the inflow and outflow of fluid which was of sufficient degree probably to prevent entirely the entrance of fluid into the lung.

CASE REPORTS

CASE 1.—(FA-39-246.) A white male infant, weighing 3,380 Gm., was delivered naturally. It gasped several times but respiration could not be established and the heart ceased beating within a few minutes.

At autopsy the external appearance of the body was entirely normal. Inspection of the abdominal cavity revealed a defect in the left posterolateral portion of the diaphragm through which was herniated the left lobe of the liver, the spleen, and the greater part of the small intestine and colon. Inspection of the thoracic cavity showed the heart and mediastinal structures displaced to the right. The left lobe of the liver occupied a position immediately to the left of the heart, and lateral to this were the small intestine and colon. The spleen was posterior and lateral. The heart had undergone normal rotation but was displaced to the right. Upon removing the abdominal organs from the thoracic cavity, a mass resembling lung tissue (Fig. 1) was found anterior to the thoracic vertebrae and posterior to the heart in the space ordinarily occupied by the posterior mediastinum. The mass was covered with pleura and, except for blood vessels connecting it with the aorta and inferior vena cava, was free in the pleural cavity. It was in no way connected with a bronchus and received its blood supply directly from the thoracic aorta.

The histologic appearance of the right lung was approximately normal for an infant at term. The alveoli were lined by normal capillaries with a few intervening cuboidal cells. A few peripheral alveoli were expanded by air, but in the rest of the lung the alveoli were of the normal intrauterine caliber or were slightly compressed. Bronchi and alveoli were present in normal proportions.

The left lung was grossly and histologically hypoplastic. The appearance was similar to lung tissue from a very premature fetus, and alveolar development was very incomplete. In many areas the alveoli were small, were lined by a continuous layer of cuboidal epithelium or were present as solid masses not yet canalized. The major blood vessels, bronchi, and areas of cartilage were relatively increased in amount due to the incomplete elaboration of alveoli.

The mass of accessory lung tissue was very similar to normal non-aerated lung (Fig. 2). It was divided into lobules by loose connective tissue and contained normal appearing blood vessels, bronchi, and cartilage. The septa were slightly wider than usual due to a slight increase in connective tissue, but the caliber

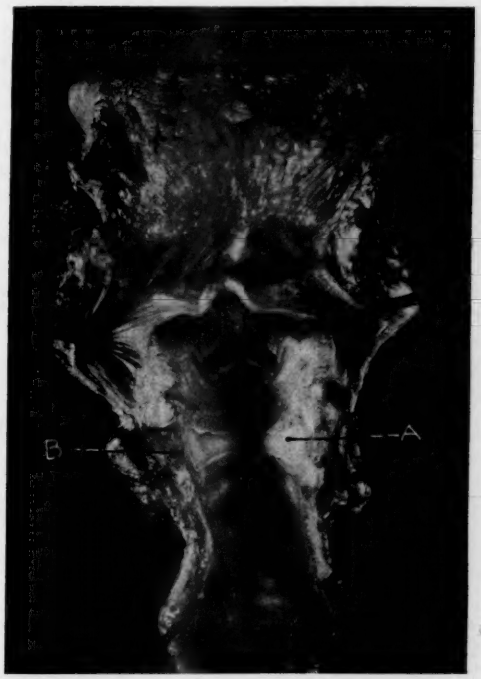

Fig. 1.—Case 1. The tongue and trachea were removed intact. The cartilage (*A*) completely occluded the trachea, and in the specimen has been split through the center. The larynx and trachea ended in round pouchlike structures, the cut surfaces of which are visible above and below the cartilage. The minute canal connecting the trachea and larynx is visible at (*B*).

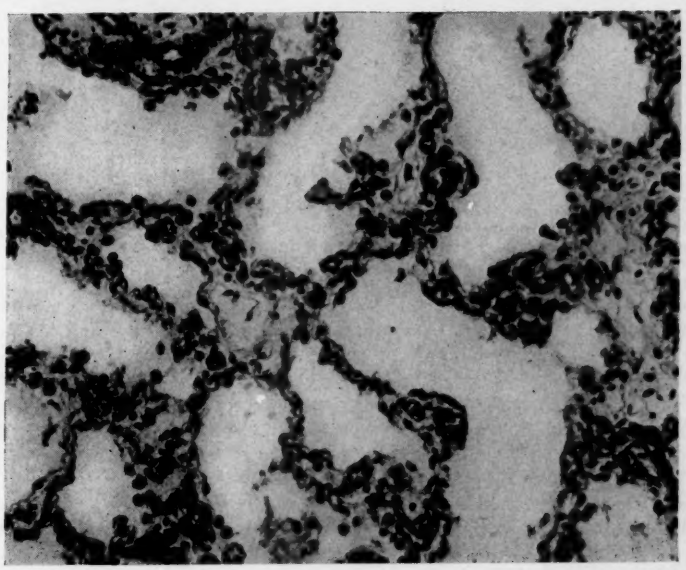

Fig. 2.—Histologic appearance of lungs from Case 1. The alveoli are normally developed. (×265.)

and shape of the alveoli were similar to normal lung. The lining of the alveoli consisted of capillaries with moderately numerous intervening cuboidal cells.

A number of cases of accessory lung can be found in the foreign literature, but few have been reported in the journals written in English. For further information the reader should see the papers of Guy and Rand,[13] Bert and Fischer,[14] and the general discussion of the subject in Abt's *Pediatrics*.[15]

CASE 2.—(FA-38-830.) A white male infant, weighing 2,630 Gm., was delivered naturally. He did not breathe and several unsuccessful attempts were made to pass a tracheal catheter. The heart ceased beating after twenty minutes.

At autopsy the external surface of the body and abdominal cavity were entirely normal. The pleural cavities, lungs, and mediastinum also appeared normal. The lungs, trachea, and tongue were removed as a single specimen, and on opening the trachea, a complete cartilaginous obstruction (Fig. 3) was found immediately below the larynx. This resulted from the imperfect formation of the cricoid cartilage which was present as a solid disc almost completely occluding the lumen of the trachea. It was not until the specimen was investigated under a dissecting microscope that a small canal approximately 1 mm. in

Fig. 3.—Case 2. The viscera have been removed from the thoracic cavity; the mediastinum has been drawn to the right and the accessory lung (*A*) has been taken out of the pocket (*C*) behind the mediastinum in which it was originally found. The blood vessel connecting the accessory lung with the aorta (*D*) is visible. The hypoplastic left lung is also present (*B*).

circumference and lined with mucosa was found posteriorly in the midline. This canal connected the two parts of the trachea and formed the only communication between the lungs and the amniotic cavity. The posterior plate of the cricoid cartilage was represented by a slight thickening of the posterior edge of the disc. The thyroid cartilage and vocal cords were both normal and the trachea below the obstruction was normal, except for a moderate decrease in the cartilage present in the tracheal rings. The lungs on cut section appeared uniform in character and fluid could be expressed from their substance.

Histologically, the lungs appeared entirely normal (Fig. 4), for an infant at term who had never inspired air. The alveoli were lined by capillaries and by irregularly distributed cuboidal cells identical with the normal pattern. The alveolar lumina were normal in size and shape. They contained a moderate

amount of precipitated protein material, indicating that fluid (probably a transudate) had been contained within them, but no vernix caseosa, desquamated epithelial cells or other debris from the amniotic fluid were present.

A study of the embryology of the larynx and trachea[16, 17] shows how this anomaly probably occurred. The laryngotracheal groove first appears in the 2.5 mm. embryo and runs lengthwise in the floor of the gut caudal to the pharyngeal pouches. This groove or ridge separates from the esophagus and becomes the larynx, trachea, and lungs. During the seventh week, the larynx is T-shaped and for a time ends blindly because of fusions of the laryngeal epithelium. This fusion varies in extent and may be complete or incomplete. Occasionally there is a fine canal that remains patent along the posterior wall of the larynx. In fetuses of ten weeks all union has disappeared. Rarely this occlusion persists and is seen at birth as a membrane or web fastened to the anterior and lateral walls and partially occluding the lumen. Our case represents a still more rare condition, in that the stenosis was cartilaginous and practically complete. The canal mentioned above also persisted.

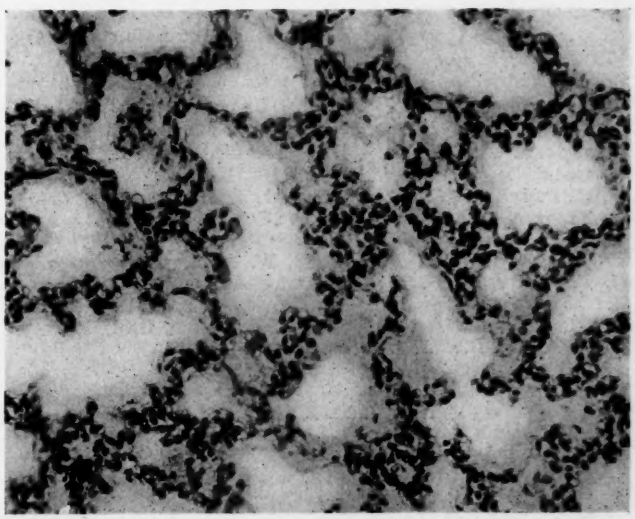

Fig. 4.—Histologic appearance of the lungs from Case 2. The alveoli are normally developed. (×265.)

Stenoses similar to the one reported here are rarely discovered, probably not so much because they do not occur as because they are incompatible with life and are not diagnosed. The incomplete stenoses are more common and usually permit adequate breathing. Many reports can be found in the literature[18-20] which discuss the etiology, diagnosis and treatment of the incomplete type.

CONCLUSIONS

1. A tidal flow of amniotic fluid in and out of the lungs is not necessary for normal alveolar development.
2. Hypoplasia of the lungs is probably caused by direct pressure on the lung parenchyma, the arrest of development being dependent on the degree of pressure suffered and the stage of development at which it is first applied.
3. There is sufficient evidence to permit the following statements:
   a. Intrauterine respiratory movements occur in laboratory animals.
   b. These respiratory movements can result in aspiration of the fluid in which the animal is immersed.

c. Intrauterine respiratory movements occur in the human fetus.
d. These respiratory movements can result in aspiration of the fluid in which the human fetus is immersed.

4. The evidence presented in the literature suggests, but does not prove, that intrauterine respiratory movements are a normal physiologic process.

The authors are greatly indebted to Dr. Aaron Gunther for the specimen of trachea and lungs which he removed at autopsy in Case 2.

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SUPRAVAGINAL AND TOTAL HYSTERECTOMY*

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THE question so often mooted as to whether supravaginal or total hysterectomy should be routinely performed cannot be answered simply. In evaluating statistical studies, the characteristics of the staff and the geographical differences in the patient population must be considered. What raises the morbidity and mortality is the extent of the disease for which the operation is performed, if other things are equal. It is the unanimous answer of those men who have served in both Northern and Southern Clinics that the latter with their large colored and rural population produce by far the "grander" fibroids and the more "magnificent" inflammatory disease. Prolapse is also almost never seen among colored patients. The operation of supravaginal hysterectomy is often reserved for the patients that present the most difficult surgical problems. By keeping these points in view, it may be possible to arrive at a conclusion unbiased by the "totalists"

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crying carcinoma of the cervical stump or by the "subtotalists" crying high operative mortality and morbidity.

The present study represents an attempt to arrive at a conclusion for this particular medical community. Because of the predominantly colored population, and because they have been accused of being responsible for high mortality rates, the statistics have been analyzed for each race. All available records of those receiving either operation and all deaths from the opening of Duke Hospital in July, 1930, to July, 1940, have been included in the study. Seven hundred and ninety-four

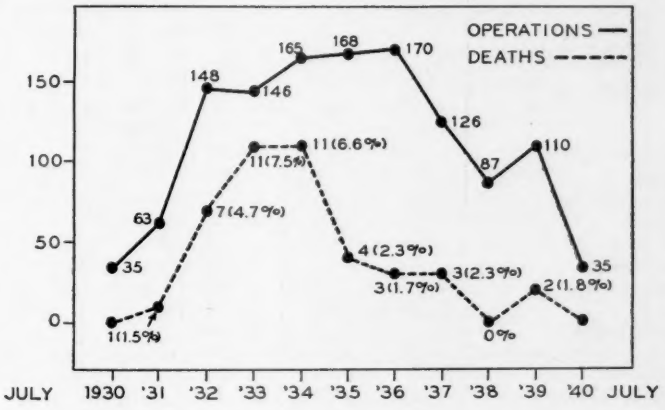

Fig. 1.

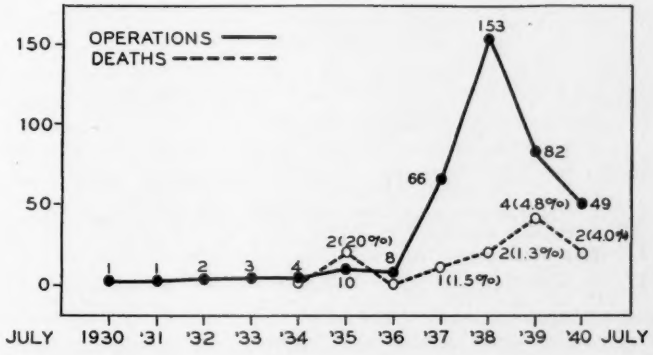

Fig. 2.

supravaginal hysterectomies and 148 total were performed on colored patients and 449 supravaginal and 225 total on white patients. Three hundred and eighty, or 21 per cent, of all operations were performed by the visiting staff and 344, or 90 per cent, of these by four men. The rest were operated upon by the house staff. This represents a total of 1,243 supravaginal hysterectomies, and 373 total hysterectomies. Prior to 1937 total hysterectomy was rarely performed for any indication other than carcinoma of the fundus. Following the trend of the times, after 1936, total hysterectomy has become almost a routine procedure on the

white patients. Largely for historical interest Figs. 1 and 2 were prepared, giving the number of patients who received operation and the mortality.

The gross mortality for supravaginal hysterectomy for the ten-year period was 3.4 per cent, for white patients 3.5 and for colored 3.3 per cent. The poor white patient with anemia, pellagra, and hypertension is no better operative risk than the anemic, obese colored patient, with

TABLE I. SUPRAVAGINAL HYSTERECTOMIES

PATHOLOGY	WHITE	COLORED	TOTAL	WHITE DEATHS	COLORED DEATHS	TOTAL DEATHS
Myoma	121	275	396	4	7	11
Myoma and infection	43	286	329	2	11	13
Infection	79	117	196	2	3	5
Normal tissue	22	16	38			
Flowing	16	10	26	1	1	2
Prolapse	46	1	47			
Previous operation	23	10	33	3		3
Hyperplasia	11	1	12			
Endometrial polyps	11	6	17			
Adenomyosis	12	6	18	1		1
Endometriosis	3	5	8			
Adenocarcinoma	3		3			
Proliferative cysts	16	12	28			
Dermoids	2	10	12			
Fibroma of ovary	4	4	8			
Therapeutic terminations	9	7	16	1	1	2
Porro sections	5	9	14	1	2	3
Tubal pregnancies	7	11	18			
Others	16	8	24	1	1	2
Totals	449	794	1,243	16	26	42

TABLE II. SUPRAVAGINAL HYSTERECTOMY FOR INDICATIONS OTHER THAN THOSE TABULATED

White:

1. Follicle cyst with hemorrhage
2. Retention cysts
3. Retention cysts
4. Adenocarcinoma of the ovary
5. Imperforate anus and congenital rectovaginal fistula
6. Double uterus
7. Blastomycosis of tube
8. Question of brucella infection in pelvis
9. Hydatidiform mole
10. Rhabdomyoma of uterus
11. Granulosa cell tumor of ovary
12. Granulosa cell tumor of ovary
13. Sarcoma arising from myoma
14. Chorioepithelioma of the tube
15. Broad ligament cysts
16. Broad ligament cysts

Colored:

1. Postoperative cervicovesicovaginal fistula
2. Tuberculosis of endometrium and myometrium
3. Adenocarcinoma and sarcoma of the uterus
4. Postoperative menstrual fistula
5. Cyst of the uterus
6. Cyst of the uterus
7. Teratoma of the ovary
8. Parovarian cysts and torsion

extensive pelvic inflammation. The gross mortality for total hysterectomy was 2.9 per cent, 2.2 per cent for white, and 4.4 per cent for colored patients. The difference will probably be explained because of the difference in vaginal flora of the two races.[1]

As in most larger clinics an attempt was made to perform the hysterectomies on patients who really needed them. Sixty-four per cent of the patients of each series received hysterectomy for myoma, myoma and infection, and infection. Tables I to IV give the pathologic bases for the procedures.

TABLE III. TOTAL HYSTERECTOMY

PATHOLOGY	WHITE	COLORED	TOTAL	WHITE DEATHS	COLORED DEATHS	TOTAL DEATHS
Myoma	54	35	89	1	1	2
Myoma infection	17	58	75		2	2
Infection	33	23	56		2	2
Normal tissue	2		2			
Flowing	10	1	11	2		2
Prolapse	31	1	32	1		1
Previous operation	8		8			
Hyperplasia	7		7			
Endometrial polyp	2	2	4			
Adenomyosis	6	4	10			
Endometriosis	2		2			
Adenocarcinoma	16	4	20	1		1
Proliferative cysts	10		10			
Dermoid	1	5	6			
Therapeutic terminations	10	7	17			
Tubal pregnancies	5	1	6			
Other	9	4	13		1	1
Carcinoma of cervix	2	3	5			
Totals	225	148	373	5	6	11

TABLE IV. TOTAL HYSTERECTOMY FOR CAUSES OTHER THAN THOSE TABULATED

White:

1. Metaplasia of the cervix
2. Previous pyometra
3. Carcinoma of the ovary
4. Fibrosarcoma of the ovary
5. Teratoma of the ovary
6. Congenital stenosis of the vagina
7. Congenital stenosis of the vagina
8. Bicornuate uterus
9. Double vagina, one stenotic, and double cervix

Colored:

1. Ruptured uterus
2. Ruptured uterus
3. Chorioepithelioma
4. Granulosa cell tumor of ovary

Those patients on whom the pathologist sent back the report of "normal" represent the class that received operation for such things as epilepsy occurring with the menses, severe dysmenorrhea in elderly spinsters, etc. A number of patients had a hysterectomy for flowing of considerable severity, uncontrollable by conservative means. The endometrium showed an entirely normal pattern and in some cases

was atrophic. Abdominal hysterectomy of either sort was used with diminishing frequency for prolapse. With such excellent operations as the Manchester and vaginal hysterectomy, the old formidable, time-consuming double procedure has become less frequently necessary.

There is another class of patients that deserves special mention, those that had been victims of piecemeal surgical procedures on pelvic organs. One patient had had six previous abdominal operations, apparently for retroversion and retention cysts. These patients have multiple pelvic complaints, and when the tissue removed by hysterectomy is reported, it is normal. More harm has been done by the performance of suspensions and meddlesome operations on infected patients than can ever be explained away in another generation. A suspension is never indicated and the "all-or-none" law should be followed in operating on inflammatory conditions if conservative management fails. Unfortunately piecemeal surgery is not performed in large clinics with critical house staffs, open staff meetings, and qualified visiting men. An institution of the United States Navy might be advantageously adopted by the medical profession and everybody in a manipulative branch of medicine be subjected to the scrutiny of a "fitness report." In the medical profession it should consist of a list of the operations performed with the report of a scrupulous pathologist on the tissue removed. This would soon stop the morning routine prevalent in so many institutions of operating on the "chronic cervicitis, chronic appendicitis, and retroversion" syndrome. The other classifications require no explanation. The three supravaginal hysterectomies for adenocarcinoma of the fundus were done because of technical difficulties in removing the cervix.

There were relatively few operations performed for proliferative cysts. Dupertuis, and Zollinger[2] in their survey of 1,000 hysterectomies done on a general surgical service, reported 632 supravaginal and total hysterectomies for myomas and 243 for cysts. In the present series the number of operations performed for retention cysts, corpora lutea, etc., is rather small.

The treatment of the adnexa during the past decade varied bewilderingly according to the operator. Usually the ovaries were not conserved in patients with infection. One operator made it routine to remove the adnexa completely with every hysterectomy. The others left one or both ovaries usually. Two of the retained ovaries required subsequent removal and one patient died following the procedure. The appendix was removed routinely from all patients in whom the blood loss had not been great nor the operation too long. Two of those that retained their appendix required subsequent operation for acute appendicitis four years later. Plastic procedures on the vagina were carried out rarely with any except the patients operated upon for prolapse. Drainage was rather frequently employed in this clinic, and about 18 per cent of those having supravaginal hysterectomy had abdominal drainage. About 22 per cent of those receiving total hysterectomy had vaginal drainage. If the drains were primarily hemostatic, to control

the bleeding or oozing from frayed peritoneal surfaces they were removed in forty-eight hours; if for frank sepsis, they were removed after seven days.

The anesthesia used is given in Table V.

TABLE V. ANESTHESIA

	GAS-OXYGEN-ETHER	ETHER	NOVOCAINE SPINAL	NOVOCAINE AND INHALATION	PONTOCAINE SPINAL	PONTOCAINE AND INHALATION	CYCLOPROPANE
Supravaginal	807	153	132	60	76	8	9
Avertin with inhalation 4, local 1, vinethene and ether 1							
Total	150	47	2		131	14	28
Epidural 1							

Novocaine spinal anesthesia was uniformly rather unsatisfactory both because of disconcerting fluctuations in blood pressure and because of the shortness of duration. Forty-four per cent of the patients receiving novocaine spinal anesthesia required supplementary inhalation anesthesia. The latter part of 1937 Dr. E. R. Rucker, an assistant resident, introduced the use of pontocaine and glucose spinal anesthesia as described by Sise[3] of the Lahey Clinic. This anesthesia has proved very satisfactory for either total or supravaginal hysterectomy. There are very few unpleasant vascular sequelae and the duration is usually ample. Only 10 per cent of the pontocaine spinal anesthesias required any supplementary inhalation anesthesia. This became rarer after the technique of Sise was generally acquired. For success all the precautions recommended by him have to be observed. None of the deaths can be counted as an anesthetic death. One case of fatal pneumonia occurred after a gas-oxygen-ether anesthesia. Fortunately gynecologists are not troubled by the pulmonary complications that make life so unpleasant for those who do gastric resections and splenectomy frequently.

Tables VI to VIII give the causes of death following the two operations. They are essentially the same for both, peritonitis, pulmonary embolism, and hemorrhage. In these latitudes where streptococcal infections are rare, where almost no erysipelas, etc., are seen, it is probable that many of the deaths due to peritonitis are secondary to some technical catastrophe. Here the staphylococcus is the predominating organism in wound sepsis and puerperal sepsis. Only one death was due to a true streptococcus peritonitis. Pulmonary embolism probably falls into the category of an unavoidable accident a little more easily than peritonitis. It has become an almost routine procedure to keep the patients in slight Trendelenburg position twenty-four hours after operation to prevent stagnation of blood in the pelvic veins and to maintain their collapse by gravity. Fatal hemorrhage occurred four times in the supravaginal group and twice in the total.

One of the latter patients deserves special mention. A 30-year-old colored patient had a simple total hysterectomy, bilateral salpingo-oophorectomy and appendectomy

TABLE VI. SUPRAVAGINAL. DEATHS AMONG WHITES

CAUSE OF DEATH	CAUSE OF OPERATION	AUTOPSY
1. Generalized peritonitis (Note: Intestine sutured to abdominal wall)	Tuboovarian abscess	Yes
2. Generalized peritonitis	Myoma and luteal cyst	No
3. Generalized peritonitis	Myoma	No
4. Acute strep. pelvic peritonitis	Myoma	Yes
5. Pulmonary embolus	Chronic nephritis. Pregnancy	Yes
6. Pulmonary embolus	Adenomyoma, endometrial polyp	Yes
7. Pulmonary embolus	Myoma, adenocarcinoma of fundus	Yes
8. Coronary thrombosis. (Note: Rt. ureter perforated)	Granulosal cell tumor of ovary	Yes
9. Sup. Mesenteric thrombosis. (Note: Avulsion of wound simultaneously)	Carcinoma of cervix, pregnancy	Yes
10. Secondary hemorrhage, uterine artery (5 hr. postoperative)	Previous operation (normal tissue)	No Abdomen re-opened
11. Secondary hemorrhage broad ligament	Previous operation (normal tissue)	No Abdomen re-opened
12. Volvulus 8 days postoperative. (Note: Avulsion of wound)	Two previous operations (corp. lut. hematoma)	No Abdomen re-opened
13. "Adynamic ileus"	Myoma. Chronic salpingitis	No
14. Intestinal obstruction 6 days postoperative	Flowing. Previous operation (normal tissue)	Yes
15. Pelvic peritonitis broncho-pneumonia	Myoma. Chronic salpingitis	Yes
16. *B. welchii* sepsis	Hydatidiform mole	Yes

under pontocaine anesthesia for chronic salpingitis. There was slight separation of the vaginal vault and she was kept in the house nineteen days after operation to receive astringent douches. Twenty-four days after operation she was admitted having a furious hemorrhage from the left uterine artery. This was fatal and autopsy reevaled necrosis and infection in the pelvic floor with perforation of the left uterine artery. Trauma was suspected but never conclusively demonstrated. There is no question that the vaginal vault after total hysterectomy is a point of lessened resistance to infection and hemorrhage. There was only one immediately fatal case of obstruction following operation and that patient, the victim of a previous piecemeal operation, had received supravaginal hysterectomy for bleeding and died six days afterward unoperated.

The different causes of death for the two procedures were relatively as follows:

	SUPRAVAGINAL	TOTAL
Peritonitis	40 per cent	27 per cent
Pulmonary embolism	16	9
Hemorrhage	8	18

These statistics must be interpreted carefully because of the small series of total hysterectomies and because supravaginal hysterectomies have been performed on the sickest patients. Possibly the indication of added danger from hemorrhage from the vault is correct in the case of total hysterectomy.

As to morbidity, the usual criteria of temperature elevation is not a valid means of determining it. There is tremendous individual variation in capacity to reaction. Most colored patients had a sharper temperature

reaction than the white. Most patients who had had a total hysterectomy ran a low-grade temperature longer than those who had had supravaginal. This was undoubtedly because of the necessarily greater spill of blood and ooze, particularly from the posterior vaginal cuff and because of the portal that the open vaginal vault affords for sepsis. In this study only those nonfatal complications that damaged the patient or prolonged her stay were considered.

Operative accidents occurred in 1.3 per cent of those patients receiving total hysterectomy and 0.5 per cent of those receiving supravaginal hysterectomy. The reason for this was the occasional greater technical difficulty in freeing the cervix and vagina from the bladder in the total procedure. The only time the ureter was damaged in the performance of supravaginal hysterectomy was in the course of removing adnexal masses. Avulsion of the abdominal wound was most common in the colored group who received supravaginal hysterectomy, 0.5 per cent. The white

TABLE VII. SUPRAVAGINAL HYSTERECTOMY DEATHS AMONG COLORED

CAUSE OF DEATH	CAUSE OF OPERATION	AUTOPSY
1. Avulsion of wound, pelvic peritonitis, obstruction	Myoma	Yes
2. Generalized peritonitis	Myoma with necrosis and infection	No
3. Generalized peritonitis	Large myoma and carcinoma of the cervix	Yes
4. Generalized peritonitis operative wound of ileum	Large myoma. Tuberculous salpingitis	No
5. Pelvic peritonitis	Myoma. Tuboovarian abscess	Yes
6. Pelvic peritonitis	Achondroplastic dwarf in labor 48 hours	Yes
7. Generalized peritonitis	Tuboovarian abscess	No
8. Generalized peritonitis	Large myoma	Yes
9. Operative wound of sigmoid generalized peritonitis	Myoma. Chronic salpingitis	Yes
10. Generalized peritonitis	Myoma. Previous operation	No
11. Operative perforation of sigmoid. Generalized peritonitis	Myoma. Ovarian abscess	Yes
12. Pelvic abscess, intestinal obstruction, bronchopneumonia	Myoma. Hydrosalpinx	Yes
13. Probably generalized peritonitis	Chronic salpingitis	No
14. Generalized peritonitis	Previous operation (flowing), normal tissue	No
15. Pulmonary embolism	Tuboovarian abscess	Yes
16. Pulmonary embolism (on table)	Myoma	Yes
17. Probably pulmonary embolism	Myoma	No
18. Emboli in pulmonary vessels, intra-abdominal hemorrhage pelvic peritonitis	Myoma, tuboovarian abscess	Yes
19. Intra-abdominal hemorrhage	Myoma. Carcinoma of the cervix	Yes
20. Shock and hemorrhage (on table)	Myoma, ovarian abscess	No
21. Bronchopneumonia (G.O.E.*)	Myoma, chronic salpingitis	Yes
22. Bronchopneumonia (spinal)	Myoma, chronic salpingitis	No
23. Operative perforation of uterus. Pulmonary infarct. Cardiac failure	Hypertension, pregnancy	Yes
24. Pulmonary edema. Cardiac failure.	Myoma. Chronic salpingitis	No
25. Pelvic peritonitis. Uremia	Ablatio placentae	Yes
26. Subarachnoid hemorrhage. Pulmonary infarct	Myoma	Yes

*Gas-oxygen-ether anesthesia.

TABLE VIII. TOTAL HYSTERECTOMY DEATHS

NO.	CAUSE OF DEATH	CAUSE OF OPERATION	AUTOPSY
		White	
1	Peritonitis	Prolapse	No
2	Peritonitis	Fibromyoma, appendiceal abscess	No
3	Pulmonary embolism	Flowing, normal tissue	No. Embolectomy
4	Primary hemorrhage	Adenocarcinoma	No
5	Intestinal catastrophe (bleeding from bowel)	Flowing, normal tissue	No
		Colored	
1	Peritonitis	Fibromyoma. Tuboovarian abscess	Yes
2	Primary hemorrhage	Ruptured pregnant uterus	Yes
3	Secondary hemorrhage from left uterine artery 24 days postoperative	Chronic salpingitis	Yes
4	Avulsion of wound 5 days postoperative. Ileus	Chronic salpingitis	Yes
5	Mania, cause unknown	Fibromyoma. Chronic salpingitis	No
6	Renal and cardial failure	Fibromyoma	No

TABLE IX. NONFATAL COMPLICATIONS ASSOCIATED WITH SUPRAVAGINAL HYSTERECTOMY ON WHITE PATIENTS

Operative accidents: Cystotomy	1
Avulsion of the wound	1
Hemorrhage: Secondary from broad ligament	1
Hemorrhage: Secondary from the uterine artery	1
Thrombophlebitis	3
Intestinal obstruction	5*
Pelvic peritonitis	1
Pelvic cellulitis	1
Pelvic abscess	1
Wound sepsis	5
Pneumonia	3
Hematuria	1
Pyelitis	1
Cystitis	5
Draining sinus	1
Peripheral abscess	1
Carcinoma of the stump	1

*Eight days, 9 days, 2 months, 5 months, 5 years, respectively.

group had 0.2 per cent for the supravaginal operation and 0.4 per cent for the total. Syphilis and diabetes were in no instance implicated. Low-grade sepsis was usually present, and there was an absence of fibroblastic response in the wound edges. Perhaps these patients were the opposites of those that obstruct and respond to low-grade sepsis by exuberant fibroblastic development.

Hemorrhage in the supravaginal group occurred secondarily and required reopening of the abdomen in two white patients. Once it was from the broad ligament as a whole and once from the uterine artery. In the total group there were four hemorrhages, all from the vaginal vault. Packing in one of these patients left her ultimately with a vaginal and abdominal fecal fistula. Four patients were delayed by failure of the vaginal vault to heal.

The true statistics on intestinal obstruction in the two groups cannot be given because of the paucity of follow-up examinations. All that can be said is that there were 15 known cases in the supravaginal group and 4 in the total group. Most of these occurred in colored patients. The longest interval following operation was five years. This is an incidence of intestinal obstruction of about 1 per cent for each type of operation, but no great significance can be attached. The other complications were about the same for each group.

TABLE X. NONFATAL COMPLICATIONS ASSOCIATED WITH SUPRAVAGINAL HYSTERECTOMY ON COLORED PATIENTS

Operative accidents	Cystotomy	4
	Intraligamentous myoma left behind	1
	Ligation of ureter	1
Avulsion of the wound		4
Shock		5
Hemorrhage: Secondary from wound		1
Thrombophlebitis		7
Intestinal obstruction*		10
Fecal fistula		1
Pelvic cellulitis		5
Pelvic abscess		2
Wound sepsis		32
Pneumonia		5
Pyelitis		5
Hematuria		2
Cystitis		1
Hemorrhage from cervix		1
Acute appendicitis 4 years later		2
Hematoma of wound		2
Infusion into thorax		1
Persistent sinus		1
Paratyphoid		1
Psychosis		1
Carcinoma of the stump		2

* Immediately postoperative 11 days, 1 month, 5 months, 10 months, 1 year, 1 year (fatal), 1 year, 9 months (due to retained Meckel's diverticulum), 4 years, 5 years.

TABLE XI. NONFATAL COMPLICATIONS ASSOCIATED WITH TOTAL HYSTERECTOMY ON WHITE PATIENTS

Operative accidents	Cystotomy	3	
	Laceration of transverse colon	1	
Avulsion of wound (one only to fascia)		2	
Shock		2	
Hemorrhage from vaginal vault		1	
Thrombophlebitis		3	
Intestinal obstruction		1	(1 month)
Pelvic abscess		1	
Pelvic cellulitis		1	
Bronchitis		1	
Hematuria		1	
Cystitis		1	
Pyelitis		1	
Hematoma of the wound		2	
Gastric distention		1	
Parotitis		1	
Radial palsy		1	
Brachial palsy		1	
Failure of vaginal vault to close		4	

TABLE XII. NONFATAL COMPLICATIONS ASSOCIATED WITH TOTAL HYSTERECTOMY ON COLORED PATIENTS

Operative accidents: Division of ureter	1
Shock	1
Hemorrhage from vaginal vault	3*
Intestinal obstruction	4†
Pelvic peritonitis	1
Pelvic abscess	3
Pelvic cellulitis	1
Wound sepsis	1
Pulmonary infarct	1
Pyelitis	1
Hematoma of wound	1

*One later developed abdominal and vaginal fecal fistulas.
†One month, twice, 5 and 11 months, 1 year and 6 months (fatal).

Three cases of carcinoma of the stump were found to have developed in patients who received supravaginal hysterectomy. This is admitted with reluctance, because only about 25 per cent of the patients have been adequately checked by follow-up examinations. The rural population and the prevalence of illiteracy were responsible. Therefore, the incidence of carcinoma of the stump in this series will later be found to be higher.

During this period, 35 patients with carcinoma of the cervical stump were seen in Duke Hospital.[1] Comparing this number with the 1,243 supravaginal hysterectomies performed simultaneously, as Meigs[4] did with the Massachusetts General Hospital series, the dubious figure of 2.8 per cent is obtained. This must be interpreted with utmost caution, because the number of hospitals in which surgery is done in this locality is large and the number of those with radiologic facilities is small. Therefore, there is a great opportunity for the nonlucrative patients with malignancy to be concentrated and the lucrative patients with surgical complaints to be scattered and treated locally.

CONCLUSIONS

It must be pointed out that no surgical procedure is without danger. Any surgical therapeutic measure is a double-edged sword and may kill as well as cure. In this clinic, the gross mortality of a small series of patients receiving total hysterectomy and a large series receiving supravaginal were essentially the same, viz., 2.9 and 3.4 per cent, respectively. This must be critically interpreted, because the less radical procedure was reserved for the poorer risks. With well-trained gynecologists the mortality for the two procedures ought to approach the same figure. Inadequately trained individuals can more safely perform the more conservative operation. In the main, it is not the operation so much as the condition demanding operation that raises the mortality rate. The vaginal vault following total hysterectomy is like the placental site of the puerperal uterus, a point of lessened resistance. Like the placental site, it is likely to bleed and become infected, and it is much closer to the peritoneum. Therefore, no gynecologist should reflexly do a total hysterectomy or a supravaginal hysterectomy. He should rather run through the prudential algebra recommended by Benjamin Franklin and decide whether the risk of excising the cervix is justified. Only by evaluating such factors as the severity of the intra-abdominal proce-

dure, the obesity of the patient, the amount of prolapse, and the condition of the cervix can he elect the proper procedure. If the cervix can be removed easily, it should be done, but supravaginal hysterectomy should by no means be abandoned.

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A STUDY OF ONE HUNDRED AND FIFTY CONSECUTIVE CASES OF ECTOPIC PREGNANCY*

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THIS report comprises a study of 150 consecutive ectopic pregnancies of less than twenty-eight weeks' duration. They occurred in the service of the Medical College of Virginia Hospitals during the ten years from Jan. 1, 1930, through 1939. This is an incidence of 1.46 per cent of the total obstetric admissions.

During the same period, there were ten extrauterine pregnancies of more than twenty-eight weeks' duration. The late extrauterine pregnancies present a different problem, and will be reported in another paper.[1-4]

The Medical College Hospitals serve not only Richmond but a large industrial and rural territory from which only abnormal cases are usually hospitalized. Therefore, the high incidence of ectopic gestation reported by us cannot be considered the average for Richmond.

In our patients it seems probable that endocrine dysfunction deserves more study as a cause of relative or temporary sterility than salpingitis. Twenty-six per cent of the women had previously aborted and 20 per cent had been sterile five years or more. Definite evidence of salpingitis was found in 22 per cent, and only 2 patients had previously been operated upon for ectopic pregnancy.

ANALYSIS OF MATERIAL

There were 59 white and 91 negro women. From the operative notes there were 2 ovarian pregnancies and 1 interstitial pregnancy. Some of the records failed to state the location of the rupture in the tube, and no classification of this type was attempted. Most of the women were admitted after the tube had ruptured. Often the patient had been sick two or three weeks, and pelvic inflammatory disease was frequently the complication that had to be ruled out after hospitalization.

Forty per cent of the patients presented no particular diagnostic problem, and were operated upon within twenty-four hours after admission. An additional 13 per cent were operated upon within the next twenty-four hours. Appendicitis was

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the original diagnosis in 8 patients. In almost 50 per cent of the other patients, the primary or second diagnosis was old pelvic inflammatory disease. Six per cent of the patients were in the hospital three weeks or more before operation.

A positive diagnosis of an early unruptured ectopic gestation is difficult to make. The patient with a recently ruptured tube, and the typical picture of internal hemorrhage, rapid pulse, increasing leucocytosis, decrease in red blood cells and hemoglobin usually offers no great diagnostic problem, and immediate operation is indicated. In the neglected case with symptoms of several weeks' duration, the differential diagnosis is a real problem, and a study of our cases gives some information that may be of value.

TABLE I. AGE

Total Number of Cases 150; White 59, or 39.33 per cent; Negro 91, or 60.66 per cent

AGE (YEARS)	PATIENTS (NUMBER)	PER CENT
Under 20	13	8.66
20 to 25	38	25.33
25 to 30	47	31.33
30 to 35	30	20.00
35 to 40	19	12.66
40 or over	3	2.00

Table I shows that 76.66 per cent of the patients were between the ages of twenty and thirty years. Only 8.66 per cent of the women were less than twenty years old and 14.66 per cent were more than thirty-five years old. The ratio of white to negro patients was about the same as that found in the total admissions.

TABLE II. MENSES

	NUMBER PATIENTS	PER CENT
No amenorrhea	76	50.66
Missed one menstrual period	42	28.00
Missed two menstrual periods	25	16.66
Missed more than two menstrual periods	3	2.00

The importance of an accurate menstrual history may be seen in Table II. Seventy-six patients denied any amenorrhea, but a careful analysis of the histories of these women shows that frequently the menses had been delayed, scant, or irregular. Seventy-eight per cent of the patients had menstruated regularly or missed only one menstrual period. Only 2 per cent of the group had missed more than 2 menstrual periods.

TABLE III. VAGINAL BLEEDING

	NUMBER PATIENTS	PER CENT
Abnormal menstrual periods	40	26.66
Spotting	18	12.00
Intermittent bleeding	79	52.66
Continuous slight bleeding	21	14.00
Profuse	7	4.66
No bleeding	39	26.00

The difficulty one encounters in correctly classifying vaginal bleeding in the presence of ectopic gestation may be seen in Table III. Seventy-four per cent of the patients had vaginal bleeding, usually scant, but 11 per cent gave a history of having passed small clots 1 cm. or less in diameter.

Table IV shows that 72 per cent of the patients complained of cramplike pain, and 82 per cent had either cramplike or dull aching pelvic pain. The classic history of sharp pain and fainting was obtained in only 17 per cent of the women. Low abdominal or pelvic tenderness was noted in 122 patients, 80 per cent. Severe pelvic tenderness was observed in 48 patients. A pelvic mass was palpated in approximately two-thirds of the patients.

TABLE IV. PAIN

	NUMBER PATIENTS	PER CENT
None	2	1.33
Shoulder pain	3	2.00
Dull ache	16	10.66
Cramp	108	72.00
Sharp with fainting	26	17.00
Sharp without fainting	47	31.33

TABLE V. TEMPERATURE (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 99	39	26.00
99 to 100	44	29.33
100 to 101	43	28.66
101 to 102	21	14.00
102 to 103	3	2.00

In Table V the temperature was below 100° F. in 55 per cent of the women, and below 101° F. in 84 per cent of all the patients. It is interesting to note that the temperature was 102° F. or above in only 2 per cent of the cases.

TABLE VI. BLOOD PRESSURE SYSTOLIC (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 70	6	4.00
70 to 80	8	5.33
80 to 90	6	4.00
90 to 100	11	7.33
100 to 110	24	16.00
110 or above	81	54.00
Not recorded	14	

The admission blood pressure is shown in Table VI. In only 36 per cent was the systolic pressure below 110. Twenty per cent of the patients were in shock when admitted.

TABLE VII. PULSE RATE (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 80	4	2.66
80 to 90	46	30.66
90 to 100	33	22.00
100 to 110	34	22.66
110 to 120	9	6.00
120 or above	24	16.00

In Table VII the pulse rate on admission was below 80 in less than 3 per cent of the patients, and between 80 and 110 in 74 per cent. This increase in pulse rate was greater than one would expect with the temperature and slight leucocytosis in this group of women.

TABLE VIII. WHITE BLOOD CELL COUNT (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 10,000	54	36.00
10,000 to 15,000	53	35.33
15,000 to 20,000	26	17.33
20,000 or above	13	8.66
Not stated	4	2.66

Thirty-six per cent (Table VIII) of the patients had a leucocyte count below 10,000, and 71 per cent below 15,000. The leucocyte count increases in the presence of intraperitoneal hemorrhage, but apparently subsides rapidly after hemorrhage stops. In salpingitis or infection secondary to abortion, the white cell count remains elevated or decreases slowly.

TABLE IX. RED BLOOD CELL COUNT (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 2 million	11	7.33
2 to 3 million	43	28.66
3 to 4 million	47	31.33
Above 4 million	31	20.66
Not stated	18	12.00

The red cell count on admission was below two million in only 7 per cent of the patients as shown in Table IX. In this group the rupture had been recent and the hemorrhage severe. The erythrocyte count was three million or above in 51 per cent of the patients.

TABLE X. HEMOGLOBIN (ADMISSION)

	NUMBER PATIENTS	PER CENT
Below 50 per cent	29	19.33
50 to 60 per cent	28	18.66
60 to 70 per cent	27	18.00
70 to 80 per cent	30	20.00
80 per cent or above	29	19.33
Not stated	7	4.66

Table X shows the hemoglobin was below 50 in 19 per cent of the patients. A rapid decrease in hemoglobin is often more important than the initial reading. When this decrease is associated with a rapid drop in red cell count and increase in leucocytes, it is very suggestive of internal hemorrhage.

TABLE XI. CONDITION OF PREGNANCY AT TIME OF OPERATION OR AUTOPSY

	NUMBER PATIENTS	PER CENT
Tube ruptured	136	80.66
Free blood in peritoneal cavity	97	64.66

Table XI shows that the patient with an ectopic pregnancy seldom seeks medical care unless she has pain or some discomfort. The presence of these symptoms indicates extravasation of blood into the peritoneal cavity or a ruptured ectopic in 9 out of 10 cases.

TABLE XII. DIFFERENTIAL DIAGNOSIS, PREOPERATIVE

	NUMBER PATIENTS	PER CENT
Pelvic inflammatory disease	50	33.33
Tuboovarian abscess	37	24.66
Ovarian cyst	20	13.33
Appendicitis	8	5.33

A positive diagnosis of ectopic pregnancy was easily made before operation in 40 per cent of the patients. In 60 per cent the preoperative diagnosis was questionable and the other diagnoses recorded either alone or with ectopic gestation are shown in Table XII. Evidence of pelvic inflammatory disease was found in 34 patients, 22.66 per cent.

TABLE XIII. TRANSFUSION

	NUMBER PATIENTS	PER CENT
500 c.c. whole blood (citrate 11, multiple syringe 33)	44	29.33
1,000 c.c. or more whole blood (citrate 2, multiple syringe 16)	18	12.00
Auto transfusion	1	0.66

Table XIII shows that 40 per cent of the patients were transfused. The method used for each patient is stated, but the figures do not indicate the total number of transfusions.

COMMENT

The mortality rate in this study is high. Twelve patients, or 8 per cent, died. Four women died before operation, and correcting for these, the operative mortality rate is 5.4 per cent. Most of the patients were on the hospital wards, and all of the deaths occurred in this group.

It is of interest to note that two patients died on the operating table before operation, and just before a transfusion was ready. This indicates that it is unwise to delay operation until the patient is out of shock. Another patient died before a donor could be obtained. The fourth woman died from pelvic cellulitis, but at autopsy an old ruptured ectopic pregnancy was found. If the diagnosis is ruptured ectopic pregnancy, immediate laparotomy and removal of the pregnant tube is indicated. Transfusion and other measures to combat shock should be carried out during the operation.

Eight women died after operation. Three of these deaths resulted directly from hemorrhage and shock. These patients were given transfusions of whole blood, but they were in such poor condition that they failed to respond. One death was due to thrombosis of the femoral veins and atelectasis. Another death was due to arsphenamine poisoning.

Three other deaths resulted from peritonitis, and in 2 of these, the operation was for peritonitis and not ectopic gestation.

SUMMARY AND CONCLUSIONS

1. One hundred and fifty cases of ectopic pregnancy have been reported, with a mortality rate of 8 per cent. This could be reduced to an operative mortality of 5.41 per cent by eliminating four patients who died before operation.

2. A complete and accurate history is most valuable in arriving at a correct and early diagnosis. The menstrual history is particularly important, and often the patient states that her last period was delayed, scant, prolonged, or abnormal. Careful inquiry will reveal a period of amenorrhea, that is, a cycle of more than twenty-eight days before the vaginal bleeding was noticed.

3. A dull ache or cramplike low abdominal or pelvic pain was recorded in 82 per cent of the patients.

4. A typical history with sudden pain, syncope, and shock was obtained from only 26 of the patients, 17 per cent.

5. Thirty-one patients, 20.66 per cent, had been sterile five years or more.

6. Thirty-nine patients, 26 per cent, gave a history of one or more abortions.

7. The temperature usually shows slight elevation, rarely above 100° F. It was below 99° F. in 39, or 26 per cent, and below 100° F. in 83, or 71 per cent, of the patients.

8. A decrease in hemoglobin and red blood cell count, associated with recurring pelvic pain and temporary leucocytosis was frequently observed. The leucocyte count was below 10,000 in 54, or 36 per cent, and above 15,000 in only 25 per cent of the patients.

9. The sedimentation rate was of value when pelvic inflammatory disease was suspected. A rapid rate is seldom seen unless infection is present. Massive hemorrhage may occasionally increase the rate.

10. Manipulation of the cervix usually causes excruciating pain in the presence of ectopic gestation.

11. Posterior colpotomy is seldom necessary.

12. Pelvic examination must be gentle.

13. Fifty per cent of the deaths could probably have been prevented if the women had consulted a physician and entered the hospital at the onset of symptoms.

14. Immediate operation, transfusion with whole blood, and other supportive measures, give the best results.

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PLACENTA BILOBATA*

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PLACENTA BILOBATA is one of a series of variations in placentation which has great practical significance, yet has received little study. In an extended investigation of the form of all placentas delivered at the University of Georgia School of Medicine, 355 bilobate placentas have been recovered.

An analysis of correlated facts now seems to indicate the major causal factors of the condition and these, for the most part, do not support previous theories bearing on the subject.

HISTORICAL REVIEW

Walder[1] reported one case in which one lobe was on the anterior wall and the other on the posterior wall of the uterus. He explained the condition as due to pathology of the mucosa from old inflammation with endometrium inadequate for production of a discoid placenta and the resulting spread of chorionic invasion to other parts. He admits no proof of the idea.

Podleschka[2] offers a rather complicated classification of the rarer-shaped human placentas. He reported the cases of a very rare type which he called placenta duplex, only one or two of which we have seen. There were no history or signs of preceding inflammatory processes in regard to his specimen, which consisted of two completely separated discoid placentas with a bridge of membranes between, measuring 7.5 cm. at the narrowest place, the cord inserting into the membrane bridge between. He also described a case with two lobes of nearly equal size but connected by a bridge of tissue. He did not give the intrauterine site of the various portions. He stated that Ahfeld thought that one portion was located on the anterior and the other on the posterior wall, and that Gott-

*Presented at the Fourth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Jacksonville, Florida, February 8, 1941.

shalk assumed that these resulted from nidation of the ovum in the lateral border of the uterus with development of the placenta on both anterior and posterior walls. He declares that Ribemont-Dessaignes considered the condition as evidence of atavism, in that the placenta on both walls approached the type found in certain monkeys. He states that Bumm[3] and Schiffman[21] assumed double nidation in their cases. He also states that Lahm[4] disagrees with these ideas in that his study of pregnancy at the third month always revealed a discoid placenta. Podleschka's own view approximates that of Walder in that he thinks the anomaly of placental shape results from nutrient variations in the endometrium in its adaptability for chorionic invasion. He also hints that the villi located in the decidua capsularis may grow on through and invade the opposite wall.

Itzkin[5] described a bilobate placenta of nearly equal lobes, one on the anterior and one on the posterior uterine wall. He also described one similar to the duplex placenta of Podleschka. In his case there was a 7 cm. bridge of membranes between

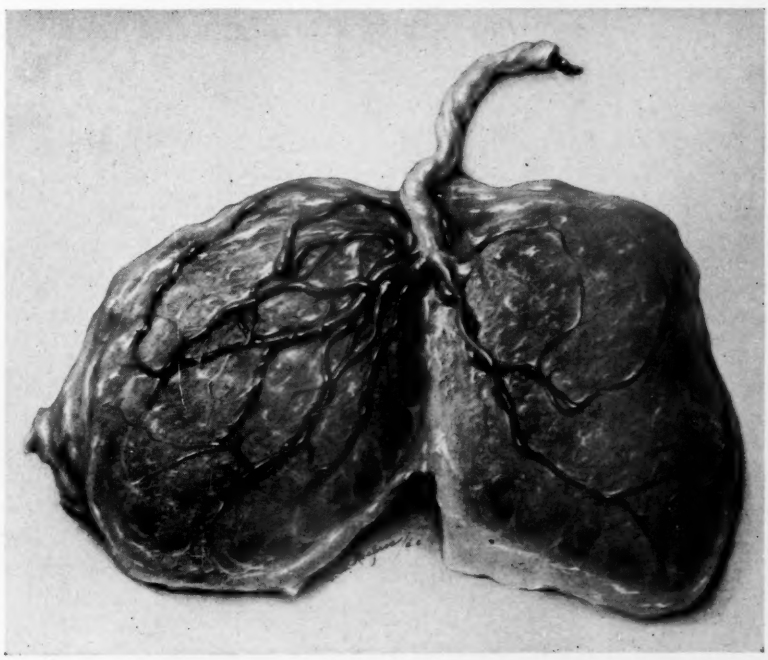

Fig. 1.—Typical bilobate placenta of equal lobes, one lobe from the anterior and one from the posterior uterine wall. The line of demarcation lay over the lateral sulcus of the uterus which separates the two walls. The cord insertion is typical in that it was inserted into the region of the demarcation.

the two discoid portions 15 and 20 cm. in diameter, respectively, the cord having inserted into the larger of the two. The bridge was over the fundal sulcus or fissure, and the two disks lay one on the anterior wall and one on the posterior wall of the uterus. Itzkin rejects both the mechanical and the atavism theory in favor of the inadequate decidua theory, and maintains that poor decidua compels the chorionic villi to spread to other parts.

Roest[6] reported the case of a bilobate placenta of nearly equal lobes. However, in his case, the cord inserted probably on the opposite side of the uterus inasmuch as the velamentous insertion was 14 cm. from one and 15 cm. from the other lobe. He gave no intrauterine position of the two lobes.

Levy[7] reported the history of a case of dystocia due to bilobate placenta located in the lower uterine segment, one lobe of which apparently prematurely separated and blocked the birth canal.

DESCRIPTION OF MATERIAL

The term bilobate is used, because in almost all of the extra-lobed placentas, there is usually only one accessory lobe in addition to that of the primary placenta (Fig. 1) to which most frequently the cord is attached, although in a few cases there may be two or more extra lobes. In most instances the extra lobe (Fig. 3, 1191) is very small in comparison with the main portion of the placenta which is usually discoid shaped. In some cases the extra lobe equals in size the primary placenta (Fig. 3, 1735), but in most cases the extra lobe is sessile to or connected to the primary placenta by a narrow neck of placental tissue in the chorion. In some specimens the lobes are separated by membranes through which run the fetal blood vessels supplying the extra lobe or lobes, and in these the condition is known

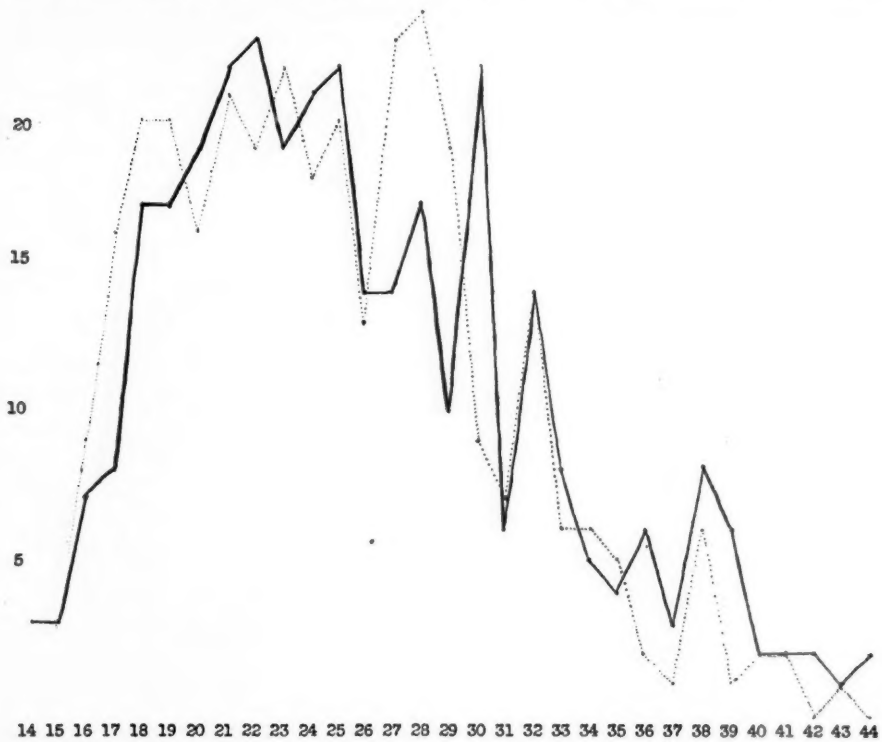

Fig. 2.—The age incidence curve of bilobate placentas is given by the continuous line. The broken line gives the age incidence in a similar group. The horizontal numbers represent the age of the patients. The vertical numbers represent the incidence in each age group.

as placenta succenturiate (Fig. 3, 2381). In 3 of our cases there were single succenturiate lobes, usually small, and in 3 others there were two succenturiate lobes with each placenta. A tabulation of the 389 extra-lobed placentas, including a few not in this study, revealed a single extra small lobe 4 or 5 cm. in diameter sessile to or connected to the placenta by a narrow neck of placental tissue in 166 cases (42.5 per cent). The extra lobe had an area of about one-third or one-half of that of the primary placenta in 123 cases (31.5 per cent), and there were 84 placentas with two essentially equal lobes, 21.5 per cent. In 16 cases (4 per cent), there were two extra lobes (Fig. 3, 2009).

The margin of the placenta deserves some attention as to whether it is normal, marginate, or circumvallate, and a record was made in each case as shown in the outline drawings. Placentas with normal edge were recorded in 250 cases. There was margination with a narrow white necrotic band on the fetal surface at the

circumference in 105 placentas (Fig. 3, 1332). This, as a rule, occurred in the larger lobe and generally on the side opposite to the small lobe. In 7 cases the marginate band of necrosis appeared in the small lobe only, and in 5 cases it appeared in both lobes. The margination appeared in one-eighth of the circumference of some placentas; in others it appeared in more of the circumference, and in 18 placentas the whole edge of the larger lobe was marginate.

STUDY BY FETAL SAC DISTENTION METHOD

A study of these placentas was made by a technique formerly described by the senior author.[8, 9] For convenience the method may be given here:

"If care is exercised in delivering the placenta it is possible to obtain the placenta and fetal membranes quite intact so that the sac is complete with the exception of the opening over the cervical area through which the fetus emerged at birth. Now by the simple procedure of submerging this sac in a tank of water up to the cervical rupture and then introducing into the cavity of the sac a known quantity of water to fill and distend it to its capacity, it is found that the sac assumes the exact shape of the distended uterus from which it came. The sac takes on a rough pyriform shape and, most remarkable of all, in most cases it develops more or less pointed bulges opposite each other at the widest part and farthest from the cervical tear. Without a doubt these correspond to the areas over which the tubes arise. This assumption is furthered by the fact that several unopened pregnant uteri, hardened in formalin, when bisected revealed the identical bulges over these areas."

There were 131 of these bilobate placentas with membranes intact enough for study by this method, from labors at term, and 16 from abortions or premature labors. Clay models made to scale were constructed for each of these, and the placenta was depicted thereon. These are illustrated in Figs. 3 and 4. The outline of the uterus appears in each case as an anterior or posterior surface view. The cervical end is readily recognized and is apparent in most cases. It will be noted that in the great majority of cases the secondary placental lobe extends across the lateral sulcus, separating the anterior and posterior flat surfaces. This point is illustrated by drawing the extra lobe as though it were lifted off of the opposite wall and extended out into space. This suggests that extension of placental tissue over this sulcus results in bilobation, but tabulation revealed that quite as many placentas lay across the sulcus at the apex of the fundus as across the two side sulci combined.

THE POSITION OF INSERTION OF THE UMBILICAL CORD

The umbilical cord was inserted into the center of the major (primary) lobe in about 50 per cent of the cases, into the major lobe eccentrically in 18 per cent, and into or near the line dividing the two lobes in 30 per cent. In about 2 per cent there was velamentous insertion. It should be noted that the third type of cord insertion is more common if the lobes are nearly equal.

PLACENTAL THICKNESS

These placentas were studied by obtaining the index weight in grams divided by the area in square centimeters (Table I). This gives approximately the average thickness in centimeters. The weight was that of the superficially washed placenta, fetal membranes, and cord. The area in square centimeters was obtained by determining the area enclosed in the outline of the placenta on a glass plate pressed firmly against the placenta on a plane surface. Similar pressure was exerted in each case so that comparable results were obtained. Table I shows that as a rule the greater the area of the lobate placenta, the less the thickness. The main exception was in the case of the placenta of the largest area of all which also weighed the most of any bilobate. This placenta, illustrated in Fig. 3 (No. 804), had an area of 552 sq. cm. and weighed 1,039 Gm. It covered almost all of both anterior

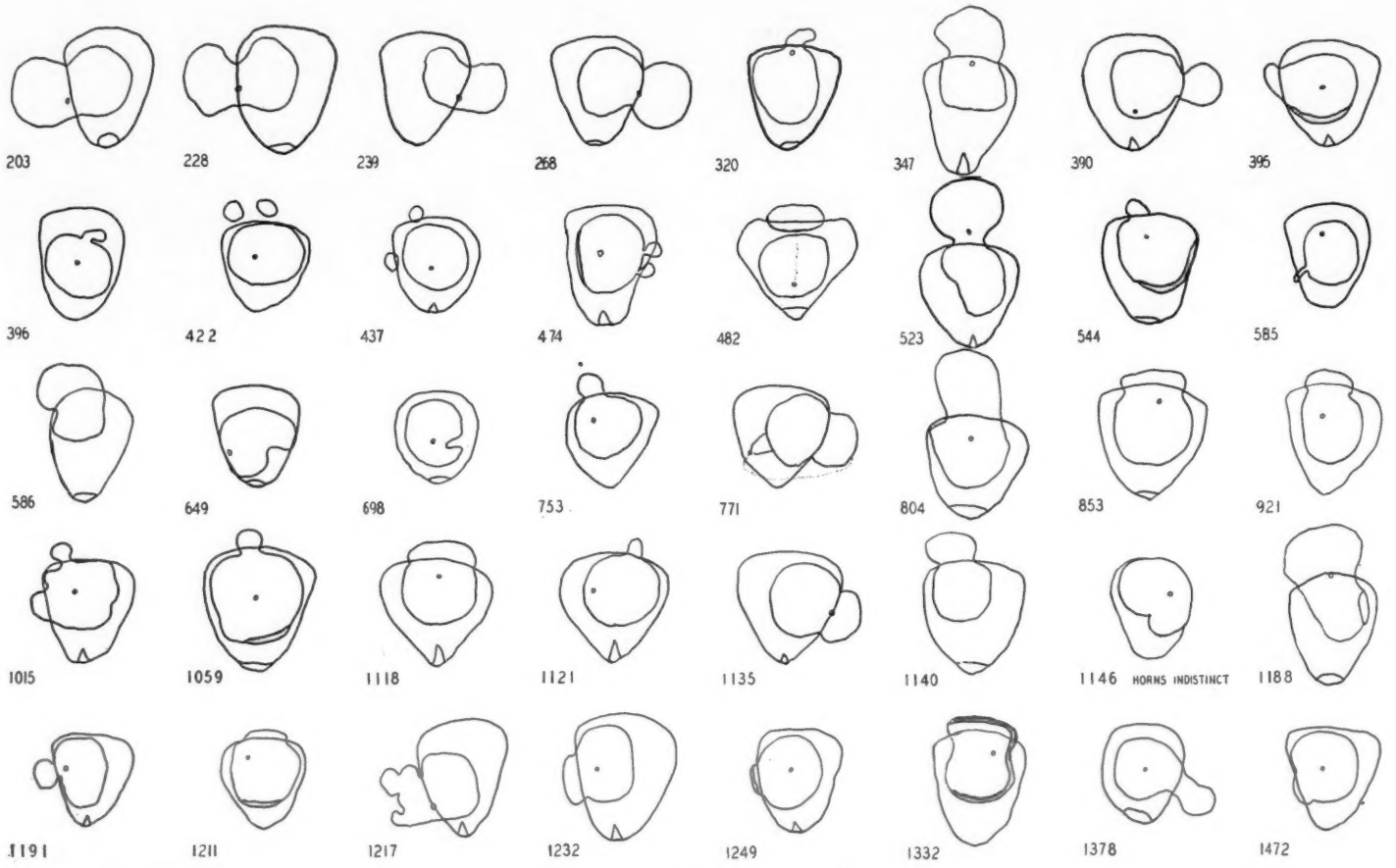
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Fig. 3.

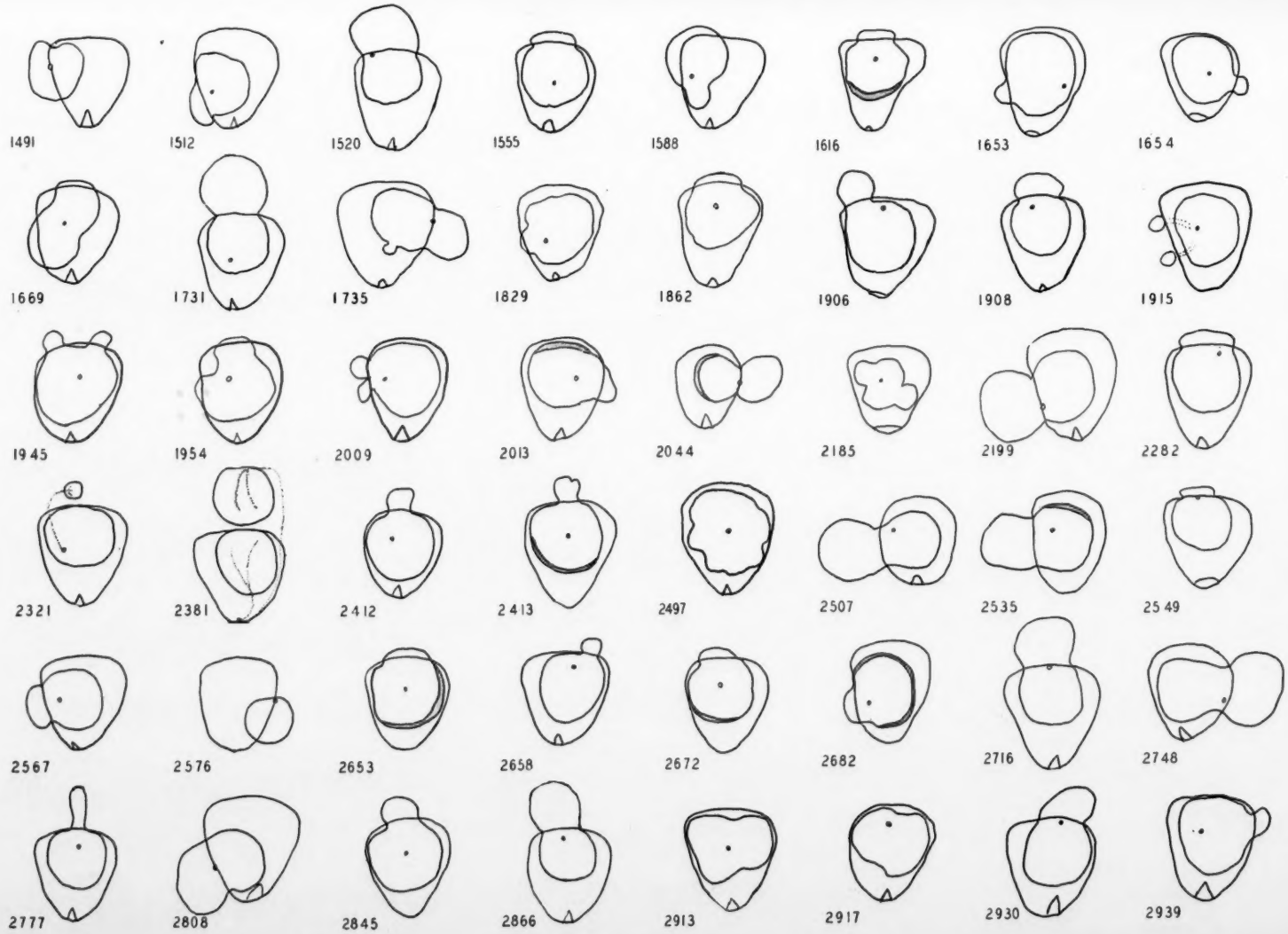
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Fig. 3—Cont'd.

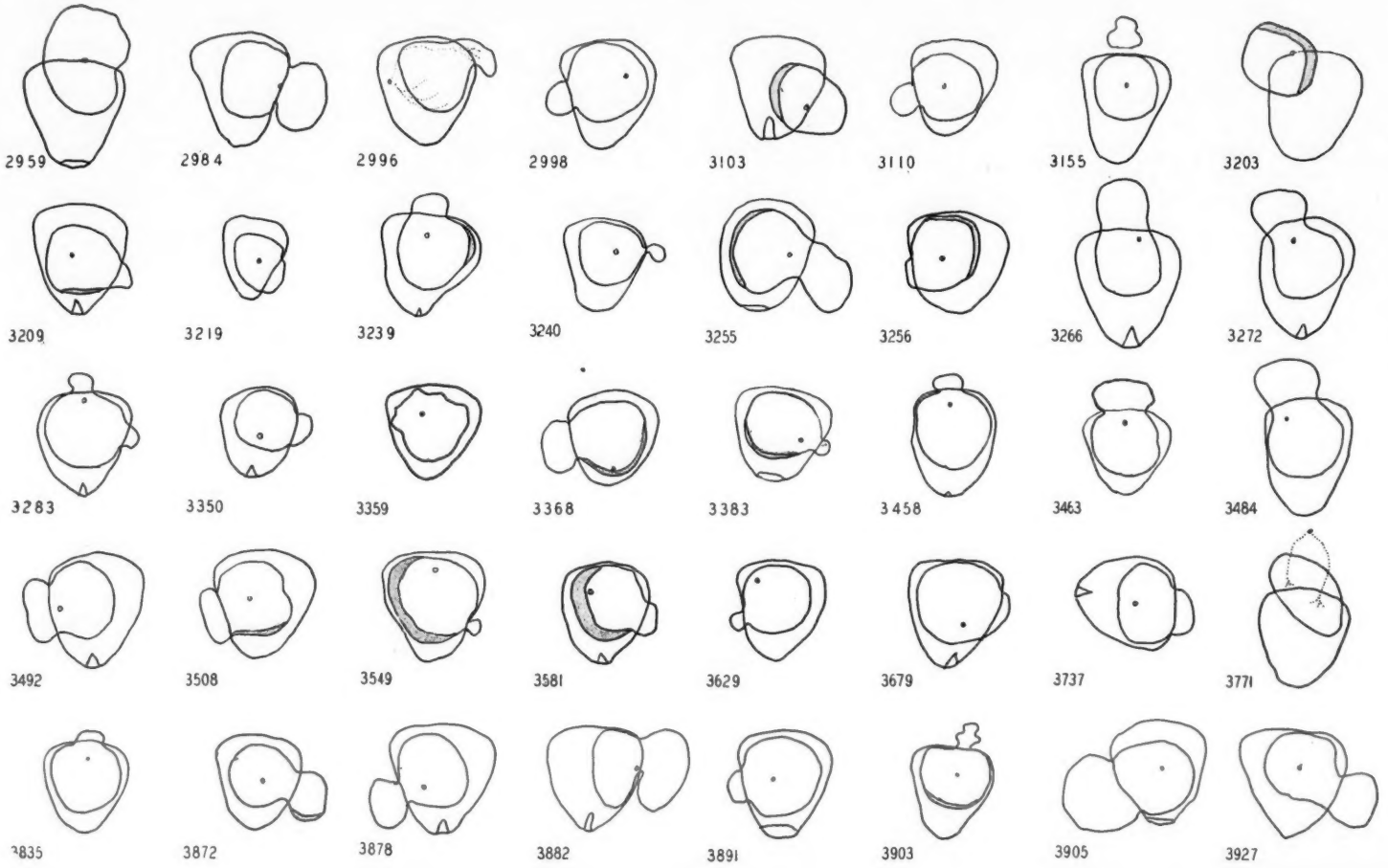
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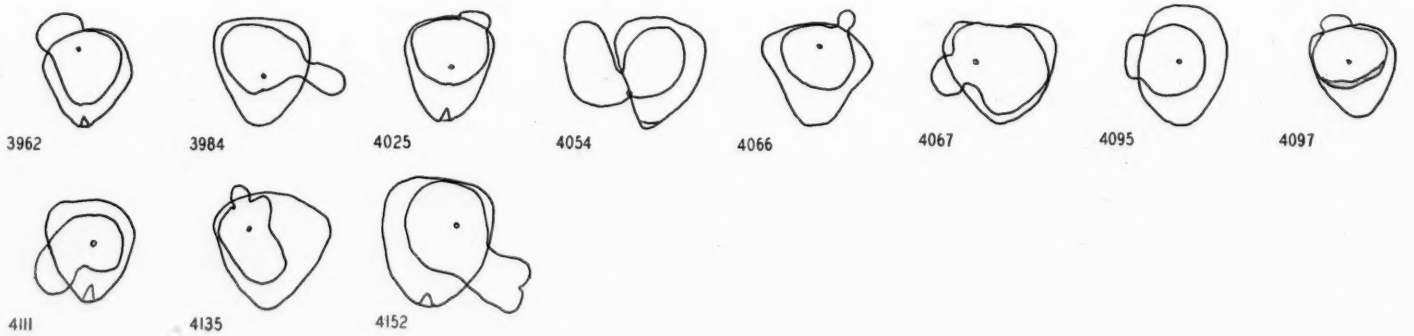
Fig. 4.



ABORTION & PREMATURE LABOR SACS

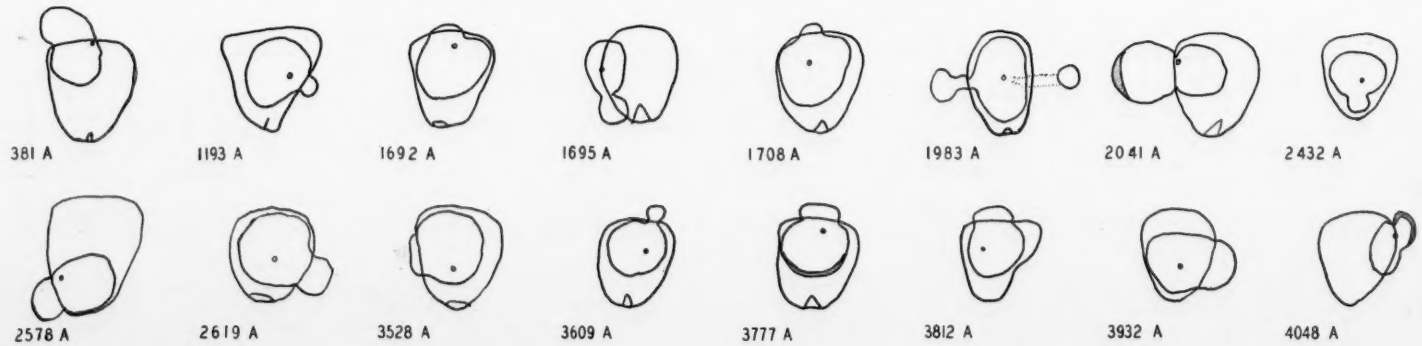


Fig. 4—Cont'd.

and posterior walls, and the two lobes connected over the fundal apex. The infant in this case weighed 8½ pounds at birth, and there was no hydramnios. The placenta covered about 45 per cent of the area of the fetal sac. The average placental coverage at term in all types is about 25 per cent.

TABLE I. SHOWING FREQUENCY RELATION OF SURFACE AREA AND THICKNESS IN 127 MATURE LOBATE PLACENTAS

AREA IN SQUARE CENTIMETERS							
200-250	250-300	300-350	350-400	400-450	450-500	500-550	550-600
1.66	1.26	1.47	1.85	1.33	1.49	1.49	1.88
2.38	1.72	1.76	1.58	1.72	1.86	1.32	
1.60	1.79	1.97	1.75	1.78	0.36	1.47	
1.69	1.66	1.76	1.51	1.91	1.41		
	1.64	1.51	1.40	1.52			
	1.79	1.49	1.77	1.57			
	2.21	2.21	1.81	1.50			
	2.31	1.48	1.50	0.92			
	2.09	2.26	1.83	1.48			
	1.54	1.26	1.66	1.75			
	1.79	1.76	1.78	1.25			
	1.24	1.39	1.75	1.94			
	1.70	1.89	1.54	1.73			
	1.56	1.98	1.83	1.42			
	1.64	1.70	1.48	1.42			
	1.63	1.58	1.77				
	1.43	1.30	1.62				
	2.01	1.45	1.60				
		1.54	2.20				
		1.52	1.65				
		1.48	1.62				
		1.24	1.67				
		1.87	1.67				
		1.26	1.32				
		1.58	1.49				
		1.60	1.78				
		1.84	1.41				
		1.67	1.95				
		1.72	1.11				
		1.53	1.83				
		1.71	1.76				
		1.67	1.89				
		1.65	1.46				
		2.12	2.07				
		1.59	1.37				
		1.64	1.73				
		2.03					
		1.92					
		1.74					
		1.48					
		1.86					
		1.62					
		1.52					
		1.51					
		1.95					
		2.32					
AVERAGE THICKNESS IN CENTIMETERS							
1.83	1.72	1.70	1.67	1.55	1.28	1.43	1.88

STATISTICAL TREATMENT OF DATA ON FREQUENCY, PREMATURITY, AGE AND RACE OF MOTHER

Among 4,098 placentas there were 355 bilobate placentas, 327 of which were full term and 28 from abortion or premature labors, with the fetus weighing less than 5

pounds. This is an incidence of 8.6 per cent, and this percentage holds good for full-time or abortion placentas. In this series, placental lobation occurred about 4 per cent more frequently in the white patients than it did in the negro patients. In the whole series of more than 4,000 pregnancies, there were 62.8 per cent white women and 37.2 per cent negro women. In the bilobate placental series there were 67 per cent white women and 33 per cent negro women.

The age incidence curve is given in Fig. 2 compared with the age incidence of all pregnancies in a similar group of patients.

Bilobation of the placenta was found in the 28 abortion or premature labor cases; 14 at the eighth month, 7 at the seventh month, 4 at the sixth month, 1 at the fifth month, and 2 at the third month.

DISCUSSION

The incidence of 8 per cent lobate placentas in our series indicates that this condition is far more common in human placentation and deserves much greater consideration than it has received. The identical incidence in premature labors shows that it is not per se a cause of abortion or early labor. The age group incidence is quite similar to that of pregnancy in general, and this speaks for a fortuitous etiology rather than an endometrial pathologic basis.

Our study shows quite definitely that implantation of the ovum must have taken place in or near a sulcus separating the two relatively flat surfaces of the anterior and posterior uterine walls, be this above or to the sides. Many of these specimens also bring up the question of depth of implantation into the decidua and the formation of a decidua capsularis. In regard to implantation we maintain the three following propositions: (1) Chorionic villi surrounding the implanting ovum will grow and thrive in any adequate decidual soil available on any side of the ovum. (2) Chorionic villi die and become necrotic if decidual nourishment fails or if the villi are pulled away from their original bed. (3) Villi once displaced cannot take root in other soil.

A consideration of the drawing of the individual fetal sacs and their placentas shows that most of them are located on both the anterior and posterior walls. Of these the vast majority are connected by placental tissue from lobe to lobe. In these the implantation must have been in the region of the sulcus or very near it and very superficially, so that chorionic villi implanted into the endometrium of the sulcus and likewise into that of both the flat surfaces, often more into one surface than into the other. In a few cases such as Fig. 3 (Nos. 482, 2381) and Fig. 4 (No. 3155), and in cases of Podleschka and of Itzkin there was a bridge of membranes between the two lobes (placenta duplex). Now it is possible that there was implantation in the sulcus here also with atrophy of the villi in the sulcus itself and persistence of villi in both the anterior and posterior uterine walls. However, it is much more plausible to consider that the implantation was near the sulcus, but so superficially as to implant into each wall. This is a common condition in certain monkeys which uniformly develop placenta duplex (macaque), one lobe on each wall. The only other plausible explanation is that the villi growing into the decidua capsularis then grow on through the surface, spanning the uterine cavity and into the adjacent decidua of the opposite uterine wall. According to Wislocki and Streeter,[10] in the macaque

there is marked thickening of the endometrial epithelium in the opposite wall directly over the implantation site, and after twelve days or so this is invaded by villi from the exposed abembryonic pole of the blastocyst. It will be interesting to ascertain whether anything similar occurs in the chimpanzee and in the human being. This study suggests that such may rarely occur in the human ovum implantation.

There are in addition several cases of irregular shaped placentas (Fig. 3, Nos. 2185, 2917, and Fig. 4, Nos. 3359, 2432 A) which are definitely limited to one wall, anteriorly or posteriorly. While in the extensive series, these are in the great minority, they must be explained on the basis of localized weak invasion, poor soil, atrophy and resorption of the villi due to premature separation, or infarction and necrosis of other cause.

Finally, there are a few instances in which implantation was directly in the sulcus separating the anterior and posterior walls, but the placenta in each case was discoid with little evidence of lobation (Fig. 3, No. 2576, and Fig. 4, Nos. 3103, 3203). In these cases the sulcus separating the two walls may have been very shallow and indistinct with a more or less cylindrical uterine cavity, such as have been seen in certain uteri removed at operation.

The only clinical significance that we have noted has been in those cases in which the two lobes lie, one anteriorly and one posteriorly, across the lateral uterine cavity sulcus, low in the uterus and near the cervix, to form placenta previa marginalis. We are of the opinion that such an extensive condition surrounding the cervix anteriorly and posteriorly has been mistaken for placenta previa centralis.

The following instances in which there was low implantation near the cervix are individually analyzed:

Fig. 3 (No. 649): Negro woman, aged 28 years, had a clinically diagnosed placenta previa with vaginal bleeding treated by rupture of the membranes. She delivered a normal infant, weighing 5 pounds 10 ounces.

Fig. 3 (No. 1217): White woman, aged 22 years, had low implantation without clinical evidence of placenta previa. She delivered a normal infant, weighing 8 pounds 2 ounces.

Fig. 4 (No. 1695 A): White woman, aged 32 years, had severe bleeding one month or more prior to spontaneous delivery at eight months, when she bled moderately, but blood was replaced by transfusion. She died on the second post-partum day, and autopsy revealed acute yellow atrophy of the liver. The edge of the placenta at the internal os of the cervix had a firm fibrotic necrotic retracted margin as is often found in placenta previa. The premature infant weighing 3 pounds 4 ounces was delivered by Willet forceps to the scalp. The infant died at one month of age.

Fig. 3 (No. 2199): White woman, aged 40 years, had no clinical evidence of placenta previa, and her infant was normal.

Fig. 3 (No. 2507): White woman had clinical evidence of low implantation and delivered a normal 9-pound infant.

Fig. 4 (No. 2578 A): White woman, aged 24 years, bled before delivery and had clinical diagnosis of placenta previa which was treated by rupture of the membranes. She delivered a normal premature infant, weighing 3 pounds 8½ ounces.

Fig. 3 (No. 2808): White woman, aged 22 years, had no clinical evidence of placenta previa. She delivered a normal infant, weighing 7 pounds 1 ounce.

Fig. 4 (No. 3905): White woman, aged 30 years, had no clinical evidence of low implantation. She delivered a normal infant, weighing 8 pounds 1 ounce. A study of the sac revealed low implantation complicated by hydramnios. The sac required 6,700 c.c. to distend it. The placenta weighed 692 Gm.

Fig. 4 (No. 3932 A): White woman, aged 42 years, had no clinical evidence of placenta previa. She delivered a normal premature infant, weighing 3 pounds 10 ounces.

SUMMARY

1. Previous studies of multiple-lobed placentas have been in the main confined to the report of a few cases found at the termination of labor, and from these the authors have developed the various theories as to formation.

2. From this present study of a large series by the fetal sac distention method, it has been found that most of the placentas consist of only two lobes, one of which is usually primary and much larger than the other.

3. It is also apparent that the two lobes usually lie one on the anterior and one on the posterior wall of the uterus and that the two lobes are joined together either at the side of the uterine cavity or over the apex of the uterine cavity.

4. The etiologic factor is considered to be fortuity, in that the fertilized ovum chanced to implant near one lateral or near the apical sulcus or fissure of the uterine cavity, and consequently trophoblastic invasion took place into both anterior and posterior endometrial walls, often more into one than into the other.

5. The condition has been shown to occur in abortion specimens but not relatively more often than in full-term sacs, and, therefore, it must not be a causative factor in premature onset of labor.

6. The condition has been shown to be associated not infrequently with low implantation of the placenta, forming a double type of placenta previa. This probably has been mistaken for placenta previa centralis.

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ORAL PROGESTIN (ANHYDRO-HYDROXY-PROGESTERONE) IN THE TREATMENT OF DYSMENORRHEA*

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THE experimental work of Knaus,[1] Novak and Reynolds[2] permits the conclusion that estrins augment and progestins inhibit uterine contractions. Kotz and Parker[3] found that 60 per cent of 50 patients with dysmenorrhea revealed a deficiency in corpus luteum as interpreted by the endometrial pattern from which bleeding occurred. These facts, it would seem, have provided a rational basis for the administration of progestin therapy in dysmenorrhea. On the other hand Wilson and Kurzrok[4] found that in the human being the maximal amplitude in uterine contractions occurred during the luteal phase and hence interdicted the use of progesterone therapy. Sturgis and Albright[5] relieved dysmenorrhea by inhibiting ovulation with estrins. However, further estrin therapy failed to prevent ovulation in the immediate successive period, and the dysmenorrhea recurred. This observation lends support to Wilson and Kurzrok's contention that "only women who have a corpus luteum can have functional dysmenorrhea." This maxim could not be substantiated by us.

In a series of some 75 patients with dysmenorrhea, endometrial biopsies were obtained immediately prior to, or at the onset of, menses in 53 instances. Three revealed a deficient progestinal endometrium of the mixed type. In 5 the bleeding was anovulatory, and of these 2 revealed a persistent estrogenic endometrium with a decidualike stroma response. However, in 45 of the 53 biopsies, the endometrial pattern revealed excellent progestinal response, of which several had a pseudodecidua reaction.

It would, therefore, seem illogical to administer progestin therapy to patients who have provided evidence of excellent utilization of their own corpus luteum, as reflected in their endometrial responses. In our experience this conclusion was borne out, for in general parenteral progesterone therapy proved disappointing except in those patients who showed evidence of corpus luteum deficiency. Two salient but contradictory facts are therefore apparent:

1. Painless menses occurring in anovulatory induced menstruation would seem to indict the corpus luteum!

2. Progesterone therapy proved useful in a series of patients who bled from an anovulatory or a deficient progestinal endometrium.

Urinary pregnanediol glucuronidate levels suddenly drop two or three days prior to onset of menses, as Venning and Browne,[6] Hamblen,[7] and

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Cope[8] and others have pointed out. This fact, which we have been able to corroborate, probably indicates complete cessation of corpus luteum activity and may account for the dysmenorrhea in spite of the progestinal type of endometrium from which bleeding occurred. The possibility that utilizable progestin during this deficient period could be made continuously and conveniently available through oral progestins prompted us to reopen this problem of the treatment of dysmenorrhea in spite of our previous disappointment with parenteral progestins. This communication deals with the treatment of dysmenorrhea by per oral administration of anhydro-hydroxy-progesterone. This product synthesized by Inhoffen, Longemann and Serini[9] is also known as pregneninolone. It is very potent orally and possesses progestinlike action among other biologic properties. This compound is closely related chemically to testosterone and progesterone, and has been shown to have progestomimetic activity when administered orally in immature rabbits,[10] and to produce in human beings a progestinal effect on the estrogen-primed endometrium.[11, 12] It has been used successfully to induce bleeding in cases of functional amenorrhea[13] and to control bleeding in menorrhagia.[14] It has also been demonstrated that this compound possesses estromimetic (immature rats) and andromimetic activity (capons and rats) in certain experimental animals.[15] These latter biologic properties could not be demonstrated when used experimentally in the human female.[16]

PROCEDURE

The present study is in the nature of a preliminary report, and was conducted on a series of 30 patients whose ages ranged from 19 to 39 years. Fifteen were married women, and of these only 2 had previously borne children, another became pregnant during treatment, and a fourth became pregnant immediately following cessation of therapy. Six had been sterile for two or more years. All patients were free of pelvic disease, except one who had a bilateral salpingectomy and still has a residual mass in one adnexal region. Five patients had retroverted uteri, and in 3 of these, it appeared that the uterus was infantile. In 2 others the uterus was somewhat bulkier or larger than normal. Endometrial biopsies were obtained in 17 of the 30 patients. In all but 4 instances the endometrial pattern was secretory. Of these, three had a persistent estrogenic endometrium, one had a cystic glandular hyperplasia. Biopsies were usually performed a few days prior to or on the day of onset of menses.

The 30 patients received oral progestin medication from 1 to 5 cycles, for a total of 64 cycles. Ten of these patients also received at some time or other parenteral progestin therapy. Sixteen additional patients who received progestin parenterally but not orally served as a basis for comparative study.

SIDE EFFECTS

Side reactions incident to the use of this drug were very few. Anhydro-hydroxy-progesterone was used not only in the present series of dysmenorrhea cases (30 patients), but also in other groups such as premenstrual tension, menorrhagia, etc., totaling some 45 cases. Only 2 patients complained of nausea and 1 complained of depression and slight dizziness. Cohen and Stein[17] claimed that 31 per cent of their patients complained of nausea, vomiting, abdominal pain, weakness, and dizziness or severe headache. Burge,[18] in the discussion of Cohen and Stein's paper, was at variance on this point and insisted that none of his 21 patients experienced undesirable reactions. Hamblen and his associates[14] witnessed no ill effects in their series. None of our patients developed any of the arrhenomimetic phenomena, skin rashes or acne. One volunteer dysmenorrhea-free patient was given 20 mg. for two days prior to onset of menses, and experienced a moderate degree of pelvic discom-

fort, with pains radiating down her thighs. Diminution of libido was noted in several patients in whom a tumescence of the sexual urge was manifested during the week prior to onset of menses.

DOSAGE

The dosage varied from 20 to 240 mg. per month, and was administered orally in 5 to 15 mg. doses per day for varying periods of two to twenty-two days prior to onset of the succeeding mensis. Occasionally medication was stopped several days prior to onset of the period, and on other occasions medication was carried along through the first few days of menstruation. The usual dosage was 5 or 10 mg., daily for the twelve days in the latter half of the cycle.

RESULTS

The evaluation of pain is a variable and personal factor. When the patient experienced from 80 to 100 per cent relief for the period, it was interpreted as a satisfactory result. When the relief was less than 80 per cent but more than 40 per cent, it was regarded as a partial improvement. When the relief was less than 40 per cent, it was considered as a failure. Fifty per cent of the cycles were satisfactorily relieved, 22 per cent partially so, and 28 per cent were considered as failures. Several of the patients continued to experience satisfactory results from one to several months after cessation of therapy. Frequently, patients who experienced moderate or no relief after the initial trial of therapy obtained good results with continued therapy. Then again, the results for individual cycles in the same individual often varied. It must be mentioned that premenstrual tension, mastalgias, hypermenorrhea, and menstrual headaches associated with dysmenorrhea were often relieved.

ENDOMETRIAL BIOPSY STUDIES

Oral progestin therapy did not interfere with ovulation when administered through the intermenstruum in 5 mg. doses per day. When biopsies were performed eight or ten hours after the onset of two consecutively treated but painless menses, a progestinal endometrium was obtained on both occasions. One patient with severe dysmenorrhea bled from an endometrium which was cystic glandular hyperplasia in type. She was treated with oral progestin for 2 cycles with excellent results. At the onset of mensis of the third cycle for which no therapy was administered, a progestinal endometrium was obtained. When this procedure was repeated prior to the onset of the fifth menstrual period, a progestinal endometrium was again obtained. This patient now has remained free from dysmenorrhea for six months since cessation of therapy. This is particularly noteworthy, for hitherto in her twenty-three-year menstrual career, severe cramping pain was a constant feature of every menstrual period.

ANALYSIS OF SUCCESSES AND FAILURES

At this stage, we are unable to surmise as to what physiologic action can account for the excellent results when obtained. Is it psychologic? In spite of the considerations which many investigators attach to psychogenic therapy, we feel that our control series ruled out this phase of the problem. Capsules of histaminase were administered to a group of 20 patients with dysmenorrhea for 1 to 3 cycles, and only two patients were benefited. Can the good results be due to increased progestin utilization? This question is difficult to answer. Urinary pregnanediol studies were performed on 11 patients with dysmenorrhea, and titers were obtained that were more or less similar to those of other groups. The administration of oral progestin was followed frequently by decreased urinary pregnanediol levels, whereas increased values often were obtained in the same patients when treated with estrins. Hamblen and associates,[14] have recently shown that oral progestin intake was not followed by alterations in urinary pregnanediol titers. Failures were most often encountered following the initial trial. One patient received from 70 to 180 mg. of oral progestin per month for three consecutive cycles without relief. Certain patients who obtained relief during some cycles experienced pain with other cycles. At times this was attributed to decrease in the dosages administered, at other times this was noted

following increase in dosages. Whether failures or successes depend on the relationship of oral progestin intake to meals, as yet has not been ascertained. It may well be that this steroid, anhydro-hydroxy-progesterone, should be taken with a fat meal or with bile salts to promote better absorption or utilization. The modus operandi of oral progestin in the therapy of dysmenorrhea is not as yet clear. Lackner and his associates,[19] Elden and Wilson,[20] obtained satisfactory results in certain groups with parenteral progestin therapy. This much is certain, that many patients who failed to respond to parenteral progestin therapy in our own series obtained partial to complete relief following oral progestin administration.

CONCLUSIONS

1. Oral progestin (anhydro-hydroxy-progesterone) was administered during 64 cycles in 30 patients with dysmenorrhea. Fifty per cent of the cycles were satisfactorily relieved, 22 per cent partially so, and 28 per cent were considered as failures.

2. Endometrial biopsies were performed in 17 of the 30 patients just prior to, or immediately after, the onset of menses. Excellent progestinal responses were obtained in 13 instances, and in 4 the bleeding was anovulatory.

3. Oral progestin therapy frequently was followed by relief in patients who failed to respond to parenteral progestins. Premenstrual tension, mastalgias, menstrual headaches, when associated with dysmenorrhea, often were relieved by oral progestin therapy. Concomitant abnormalities in the menstrual flow were often stabilized.

4. Response to therapy did not depend on size and position of uterus nor on dosage employed. Results were variable in the same individual. Increase or decrease in dosage was liable to be followed by pain.

5. Undesirable side reactions such as nausea, dizziness, etc., were very infrequent. The authors believe the substance innocuous if used in dosages up to 240 mg. per month. Oral progestin therapy did not interfere with ovulation. One patient became pregnant during therapy, and another immediately after cessation of therapy.

The oral progestin (anhydro-hydroxy-progesterone), used in this investigation, was kindly furnished as Pranone by W. H. Stoner, Schering Corporation. Other synonyms for this product are pregneninolone and 17-ethinyl testosterone.

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STERILIZATION IN THE PUERPERIUM*

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AN IMPORTANT factor in the reduction of maternal deaths is the prevention of pregnancy in those individuals whose physical condition makes repeated childbearing unusually hazardous. About 95 per cent of the women in the higher social and intellectual groups can successfully prevent pregnancies by the use of the various mechanical contraceptive devices. Many clinic patients, however, cannot successfully use contraceptive measures, and for these, some type of operative sterilization must be employed if rapidly repeated pregnancies are to be avoided. Contraceptive advice is given, when indicated, as a part of the routine care in our post-partum clinic. Unfortunately, only a small percentage of our public ward patients have been successful in the use of contraceptive measures, in spite of the fact that only those whom we presumed to have sufficient ability and intelligence to use the methods, were so advised.

It was generally the custom to perform sterilizing operations some months after delivery, usually as a part of a gynecologic repair operation. This required a second hospital admission with its additional expense and period of disability, and not infrequently another pregnancy would occur before the patient returned for the repair and sterilization. Some obstetricians have at times effected delivery by cesarean section, primarily for the purpose of sterilization, although we have never felt that sterilization alone was sufficient justification for abdominal delivery.

In 1932, Skajaa[1] pointed out the feasibility of performing sterilizing operations during the puerperium and reported 126 cases done between the second and twenty-ninth post-partum days. In 1939, Adair and Brown[2] reported 50 cases of puerperal sterilizations done within twenty-four hours after delivery. In 1940, Russell[3] recorded 29 cases done at intervals varying from one hour to thirteen days after delivery, and in the same year Hewitt and Whitley[4] recorded 100 cases performed one hour after delivery.

During the five-year period from July 1, 1935, to June 30, 1940, 309 sterilizations were performed during the puerperium on the Obstetrical and Gynecological Service at the University of Virginia Hospital. In the present report, we wish to present an analysis and review of these cases.

PERMISSION

Aside from the Virginia law for compulsory sterilization of mental defectives and those with presumably inheritable mental disease, there is no law in Virginia regarding contraception or sterilization. It is our custom to require a written request and permission for sterilization, to be signed by both the woman and her husband in the presence of witnesses.

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The average age of this group of 309 patients was 29.4 years, the youngest 18 and the oldest 45 years. Two hundred and forty-four were white and 65 were colored patients.

INDICATIONS

The indications for sterilization in this group are shown in Table I.

TABLE I. INDICATIONS FOR STERILIZATION

INDICATION	NO.
Excessive multiparity	175
Hypertension and/or nephritis	84
Cardiac and vascular diseases	15
Nervous and mental diseases	10
Secondary perineorrhaphy (at delivery)	9
Pyelitis and pyonephrosis	7
Miscellaneous causes (1 case each)	9
Total	309

The largest group is made up of those in whom we have given the indication as excessive multiparity. This group consists mainly of those from the lower social, economic, and intellectual group, in whom the use of even the simplest types of contraceptive materials is too complicated and expensive for them, as is proved by our experience in the post-partum clinic. Many of them are from the mountainous areas in our vicinity and most of them are completely indigent, applying repeatedly for admission to the hospital on free beds. The 175 women in this group had had a total of 1,161 pregnancies or an average of 6.63 pregnancies per woman, with extremes from a minimum of 3 to a maximum of 15 pregnancies. Hypertension and renal disease was the indication in 84 instances, all in multiparous individuals, one of whom had had 15 pregnancies. In 9 instances, a secondary perineorrhaphy was done at the time of delivery because of old lacerations and relaxations of the perineum, and was followed by sterilization in the immediate puerperium.

METHOD

There has been some discussion as to the proper time in the puerperium to perform a sterilizing operation. It is our belief that, as far as morbidity is concerned, a proper selection of cases is more important than the time at which the operation is done. We feel that the procedure should be avoided in those whose labors have been such that potential infection may be assumed to be present. We have done sterilizations at time intervals varying from a few hours post partum to the twenty-first post-partum day. The main advantage of early post-partum sterilization is the decrease in the length of hospitalization. At present we perform the operation as early in the puerperium as is feasible, dependent on the type of labor, the condition of the patient, and the presentation of the necessary permits. We do the operation at a scheduled time on regular operating days, which is, of course, impossible if the operations are routinely done one hour post partum.

The anesthesia employed seems to be purely one of personal preference and experience of the anesthetist and surgeon. We prefer spinal anesthesia, which is the anesthesia most commonly used in our hospital for abdominal surgery. Two hundred and ninety-seven of the cases were done with spinal anesthesia, using 150 mg. of procaine. Nine were done under general anesthesia and 3 under local infiltration.

Unhappily none of the methods of operative sterilization short of complete castration seem to be 100 per cent effective. The multiplicity of operative procedures, which consist mainly of various gymnastic procedures on the Fallopian tubes, attest to their lack of perfection in results. Of the 309 sterilizations in the present report, 219 of them have been done by the Pomeroy technique. Formerly with this method we used No. 1 or No. 2 chromic catgut for the ligature, but during the past year we have been using No. 1 plain catgut exclusively. Eighty-six of the early cases were done by a method which we speak of as segmental resection. This seems to be a modification, proposed by Fritsch,[5] of the Kehrer method. With this technique

a segment of the tube was excised and the proximal extremity doubly ligated with heavy black silk and the distal end singly ligated with silk. The Madlener technique was used three times and cornual excision once.

The procedure is carried out through a subumbilical incision of approximately one and one-half inches in length. Manipulation of the pelvic structures is avoided, the tube being simply exposed with a sponge stick or Babcock clamp, lifted in its midportion, identified by its fimbriated extremity, and the sterilizing procedure carried out. If the appendix is easily available it is removed. For the past year, we have been closing the abdominal incision with fine black silk.

MORBIDITY

In the 309 cases of sterilization, 66, or 21 per cent, had morbidity on the basis of the standard of morbidity adopted by the American Committee on Maternal Welfare (100.4° F. or over on any two days after the first twenty-four hours post partum, oral temperatures taken at least four times daily). Of these 66, only 12 had sufficient elevation or prolongation of fever to interfere with discharge from the hospital at the usual time. The average duration of the fever for all of the cases of morbidity was two days. Our incidence of morbidity is higher than those quoted by Adair and Brown,[2] 12 per cent, but their patients were operated upon in twenty-four hours which would eliminate elevations on the day of operation as a part of the morbidity. Our morbidity includes those elevations on the day of operation, except those that were done in the first twenty-four hours.

The complications are shown in Table II.

TABLE II. COMPLICATIONS

DIAGNOSES	NO.	DAY P. P. OPERATED	REMARKS
Endometritis	3	2, 3, and 5 days	1 version and extraction
Pyelitis	3	2, 4, and 12 days	
Pneumonia	2	9 and 11 days	1 acute appendicitis
Multiple pulmonary emboli	1	3 days	Retrocecal appendix Obesity, 218 pounds
Thrombophlebitis	1	2 days	Perineorrhaphy
Atelectasis	1	2 days	
Diabetic acidosis, pyelitis, pneumonia	1	9 days	Died
Total	12		

One death occurred in this series of 309 patients. This was a thirty-four-year old colored multipara with a severe diabetes and hypertension, for which labor was induced by rupture of the membranes, followed by delivery of an excessive-sized child. The diabetes was still poorly controlled post partum; however, she was sterilized on the ninth post-partum day. She developed pyelitis and pneumonia and went into a severe acidosis and died on the sixth postoperative day. It was an error to have sterilized her, as the diabetes was poorly controlled, and her general condition was unsatisfactory.

The one patient with thrombophlebitis had a secondary perineorrhaphy at the time of delivery and was sterilized thirty-six hours later. Phlebitis appeared on the eighth post-partum day and required a total hospital stay of thirty days. The patient with multiple pulmonary emboli was sterilized on the third post-partum day and had a total period of hospitalization of thirty-one days. Both patients with pneumonia recovered and were discharged from the hospital on the sixteenth postoperative day.

The appendix was removed at the time of sterilization in 178 of the 309 patients. In 140 of these there was no morbidity, and in the 66 instances of morbidity, the appendix had been removed in only 38. The appendix was not removed in the one fatal case. The removal of the appendix apparently had no appreciable effect on the convalescence or on the incidence of morbidity.

When the febrile cases are analyzed in relation to the time post partum that the operation was done, no constant relationship is found. This is interesting because

Skajaa,[1] Adair and Brown,[2] and Russell[3] have emphasized the dangers of sterilization after the first post-partum day. Skajaa[1] in his report had 46 patients who were operated upon between the fifth and twenty-ninth post-partum days, and in these there were 8 cases of thrombosis and embolism; 5 of them occurring in 12 cases done on the fifth and sixth days. The 2 patients with thrombosis and embolism which occurred in our 309 patients, were operated upon on the second and third days, respectively. The number operated upon on the different post-partum days with the number and percentage of cases with fever and complications for those days are shown in Table III. The time post partum that the operation is performed does not seem to be associated with any significant variations in the incidence of morbidity or complications.

TABLE III. DAY OF OPERATION WITH MORBIDITY

P.P. DAY	NUMBER OF OPERATIONS	NUMBER WITH MORBIDITY	COMPLICATIONS		PER CENT MORBIDITY
1	12	1	0		8
2	47	9	Endometritis Pyelitis Atelectasis Thrombophlebitis	1 1 1 1	19
3	64	9	Endometritis Pulmonary Emboli	1 1	14
4	47	12	Pyelitis	1	25
5	27	6	Endometritis	1	22
6	10	0			0
7	17	1			6
8	27	12			44
9	17	5	Pneumonia	2	30
10-21	41	11	Pyelitis Pneumonia	1 1	26
Totals	309	66		12	21

TABLE IV. STERILIZATIONS BY YEARS WITH MORBIDITY

YEAR	NUMBER	AVE. P.P. DAY DONE	AVE. DAYS IN HOSP. P.O.	AVE. TOTAL HOSP. DAYS	NUMBER WITH MORBIDITY	COMPLICATIONS	PER CENT MORBIDITY
1935	5	12.4	13	25	3	0	60
1936	20	9.5	9.8	19.3	7	1	35
1937	55	9.5	6.9	16.4	12	2	22
1938	75	4.8	6	10.8	17	2	23
1939	91	3.3	6.3	9.6	24	7	26
1940	63	3.2	5.1	8.3	3	0	5
Total	309				66	12	
Averages		5.2	6.4	11.7			21

In Table IV the cases are presented by years, showing the average post-partum day upon which the operation was performed during that year, the average length of postoperative stay in the hospital, as well as the number of febrile cases and complications for each year. Each year we have gradually shortened the interval between delivery and sterilization as well as the postoperative period of hospitalization. With the exception of the years 1935 and 1940, there is no appreciable difference in the incidence of morbidity. The morbidity incidence of 60 per cent in 1935 seems without significance because there were only 5 cases for the half of that year under consideration. In 1940 the interval between delivery and sterilization was essentially the same as for 1939, so there seems to be no obvious explanation in the time interval for the lower incidence of morbidity in 1940. Of the 63 cases done in 1940, the abdominal incision was closed with catgut in 25 and

with black silk in 38. The 3 cases of morbidity (12 per cent) which did occur, were in those 25 cases in which the incision was closed with catgut. There were no instances of fever in the 38 patients in whom the incision was closed with black silk. In 1940 the patients averaged a total hospital stay of 8.3 days for both delivery and sterilization, with an average interval of 3.2 days between delivery and sterilization.

FOLLOW-UP

Ordinarily it is assumed that subsequent information is unnecessary in order to determine the effectiveness of sterilization, inasmuch as the patient will undoubtedly seek out, often with some vindictiveness, the surgeon who operated upon her, in the event that a pregnancy should subsequently occur. However, we attempted to follow-up these 309 patients, and we have recently seen 107 and have had a letter from 119 of them stating that no pregnancies have occurred since the operation, a follow-up incidence of 73 per cent. An analysis of the follow-up information is shown in Table V.

TABLE V. FOLLOW-UP DATA

METHOD	NUMBER DONE	NUMBER FOLLOW-UP	FOLLOW-UP PERCENTAGE
Pomeroy	219	145	66
Segmental resection	86	77	90
Madlener	3	3	100
Cornual excision	1	1	100
Totals	309	226	Average 73

We have definite knowledge that 145, or 66 per cent, of the patients sterilized by the Pomeroy method, and 77, or 90 per cent, of the 86 sterilized by segmental resection have as yet had no pregnancies since sterilization. The 3 patients sterilized by the Madlener method and the one by cornual excision have been seen and are known not to have conceived. The patients seem quite appreciative in the answers to the follow-up letters, and except for occasional instances of menstrual irregularities, they have had no unusual symptoms. Unfortunately our letter seems to have disturbed the confidence of a few of them in the effectiveness of the operation, and will no doubt cause them some slight degree of mental anxiety for a few months.

SUMMARY

We have presented a report of 309 cases of sterilization at varying intervals from the first to the twenty-first post-partum day.

Spinal anesthesia was used in 297, general anesthesia in 9, and local anesthesia in 3 cases.

The sterilization was done by the Pomeroy technique in 219, segmental resection with heavy silk ligatures in 86, by the Madlener method in 3, and cornual excision in 1 case.

The appendix was removed at the time of sterilization in 178 of the patients, without any appreciable effect on the convalescence or on the incidence of morbidity.

Sixty-six, or 21 per cent, had morbidity on the basis of the standard of morbidity determined by the American Committee on Maternal Welfare. Only 12 of these had postoperative complications requiring prolongation of the hospital stay.

There was one death, a patient with hypertension and diabetes who developed pyelitis and pneumonia and died on the fifth postoperative day in acidosis.

The time post partum at which the operation was performed seemed to show no definite statistical relationship to the incidence of morbidity or postoperative complications.

A yearly analysis of the cases is presented which shows a progressive decrease in the post-partum interval before operation and in the total period of hospitalization with each year. During the year 1940, sterilizations were done mostly on the third day, and the patients were discharged from the hospital on the average on the eighth post-partum day. During 1940 the incidence of morbidity was only 5 per cent and in 38 consecutive cases during that year in which the abdominal incision was closed with black silk, there were no instances of morbidity or complications.

Two hundred and twenty-six, or 73 per cent, of these 309 patients have been followed up either by examination or letter, and no subsequent pregnancies have occurred in them.

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AN ELECTROMETRIC STUDY OF UTERINE ACTIVITY*

PRELIMINARY REPORT

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INVESTIGATORS have long recognized the necessity for a better understanding of the essential characteristics of human uterine behavior. Few of the methods of study have been entirely satisfactory. While much has been learned from experimental analysis, valid interpretations in terms of human physiology have been difficult. It is not surprising, therefore, that the success of the electrocardiograph and the electroencephalograph has stimulated the search for an electrical means of recording uterine activity. Two types of such procedure are available. One is to apply the techniques of recording alternating current changes in the manner similar to that of the electrocardiograph, and the other is to employ the more recently developed technique of recording changes in the direct current or standing potentials in the intact organism. The validity of either of these procedures must rest on one-to-one correlations between the changes in electrical activity and other known evidences of physiologic change.

PREVIOUS INVESTIGATIONS

Among the first attempts to record uterine activity are those which made use of manometric recording of volume changes in the uterus through flexible balloons

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(Dickinson).[1] Knaus[2] made observations on the human uterus in vivo by inserting an elastic bag into the uterus and recording uterine contractions on a kymograph. He found (a) spontaneous rhythmical contractions in regularly menstruating women during the first fourteen days, the uterus during this phase reacting to pituitary extract. (b) On the sixteenth day and lasting until menstruation begins, no spontaneous contractions occur, and the uterus does not contract with pituitrin injections. This follows according to Knaus, because of an inhibiting influence of the corpus luteum on the uterus. (c) When this failure to react to pituitrin does appear, Knaus assumes that ovulation has taken place within a definite time and used this as a means of determining the time of ovulation in the menstrual cycle. Kurzrok and others,[3] in a study of uterine motility, made by inserting a rubber balloon into the uterine cavity, filling the balloon with air and attaching it to a recording kymograph, failed to confirm the observation of Knaus. It should be noted that in these studies, Kurzrok stated that "dysmenorrhea occurs at the time when the uterine contractions achieve their greatest amplitude, i.e., just preceding and during the first few days of the menstrual flow."

Moir,[4] in a clinical comparison of ergotoxine and ergotamine, used a hydrostatic intrauterine bag to observe post-partum uterine contractions. Adair and Davis[5] observed the effects of oxytoxic drugs on the human post-partum uterus by inserting rubber bags filled with water.

Paralleling these observations by mechanical methods are a number of studies involving electrical techniques. Observations on the human uterus have been made by Theilhaber,[6] Bode,[7] Veit,[8] and Falk and Nahon,[9] making use of the string galvanometer and associated equipment.

More recently Jacobson and others[10] reported observations on electrical and mechanical activity of the human nonpregnant uterus. Inserting two electrodes into the lips of the cervix, they concluded that contraction voltages of the uterus can be studied with the string galvanometer plus amplifiers, and showed that mechanical tracings parallel those made by electrical methods. Their method is elaborate and complicated. Vozza,[11] working with rabbit uteri, also concluded that there was a relationship between mechanical contractions and bioelectric phenomena.

PRESENT METHOD

In the studies which have so far been reported, difficulties have been encountered in the rather complicated techniques or in interpretation of the findings. It seemed worthwhile, therefore, to examine the possibility of applying the Burr-Lane-Nims[12] technique for recording standing potentials to this problem. The experimental findings resulting from the application of this technique to the study of estrous phenomena in experimental animals and more particularly the exact timing of ovulation in animals and in women suggested the possibility that the technique might be useful in studying uterine physiology.

In essence the method consists of connecting a vacuum tube microvoltmeter to the cervix of the uterus and recording the changes in voltage by means of a General Electric photoelectric recorder. The instruments, if so used, are capable of recording only relatively slow changes in the standing potential of the uterus. For the majority of the readings, the recording paper was traveling at the rate of six inches per hour, although at times this could be increased to six inches per minute. Ideally, the microvoltmeter should be connected to the cervix by reversible nonpolarizing electrodes, since it is well known that metal in contact with living tissues gives rise to an unstable and artificial contact potential. With such electrodes, accurate recording of the absolute potential difference can be made with certainty. How-

ever, the technical difficulties of applying such electrodes to the cervix made it seem advisable to sacrifice the absolute value of the potential difference in favor of a procedure which would record the changes in the standing potential, even though the latter were complicated by the presence of an artificial potential.

For this reason, the microvoltmeter was connected to the patient by means of wires terminating in metal clips which gripped the lips of the cervix. In practice, the cervix was exposed through a Sims' metal vaginal speculum. The clip electrodes and the wires connecting them to the instrument were insulated by rubber covering except for the terminal jaws. The ground electrode from the microvoltmeter was inserted into the posterior lip of the cervix and the hot electrode into the anterior lip. When repeated daily observations were made on the same patient, different sites were used for attachment of the electrodes, but the same polar relationships were maintained. The electrodes were applied with the patient in the dorsal lithotomy position after which the patient was made comfortable on the operating table with legs extended. The vaginal speculum remained in place throughout the period of recording and apparently caused no distress. Activity was necessarily limited during observations, but other than backache patients had no complaints except when uterine cramps were produced by injections of pituitrin and ergotrate. A sharp pain was produced momentarily in some patients at the time of attachment of electrodes to the cervix, but this disappeared almost immediately. In general, observations were made during periods of thirty minutes to three hours, the average time being two hours. In the daily observations on one patient (R. F.) covering a complete menstrual cycle, records were kept for a minimum of two hours. The corpus luteum was in all probability functioning in this patient, for she was the mother of four children. As might be expected, the metal-to-tissue electrodes gave a somewhat unstable base line with a considerable tendency to drift. This could be obviated to some degree by including larger amounts of tissue in the bite of the clips.

In the patients who were given pituitrin or ergotrate, and in one patient, receiving estradiol, recordings were run for a period of thirty minutes to one hour, preceding the giving of the preparation, so that ample time was allowed to observe the character of the spontaneous behavior of the uterus. Pituitrin and the sex hormone preparations were administered intramuscularly; ergotrate injected intravenously.

In the cyclic study made on one patient (R. F.), injections of progesterone were given at the completion of an observation, and recordings repeated subsequent days to determine the effect on the uterus.

The menstrual cycle (in all patients having menses) was dated from the first day of the flow, this being the usual method of calculation. While some investigators[13, 14] are of the opinion that a new cycle begins three to five days after the onset of a period, it was deemed preferable to consider the first day of bleeding as No. 1 in the cycle. The study of one menstrual cycle is complete, so that conclusions can easily be interpreted by either method of calculation. No endometrial studies were made.

RESULTS

a. *Normal Case.*—In the present study, 56 sets of observations were made on 17 patients distributed as indicated in Table I. Case 1 was a 27-year-old woman, the mother of four children. The electrometric recording on successive days of one complete menstrual cycle is shown in Fig. 1. As a check on these, seven additional days from other cycles are included in the figure to demonstrate that

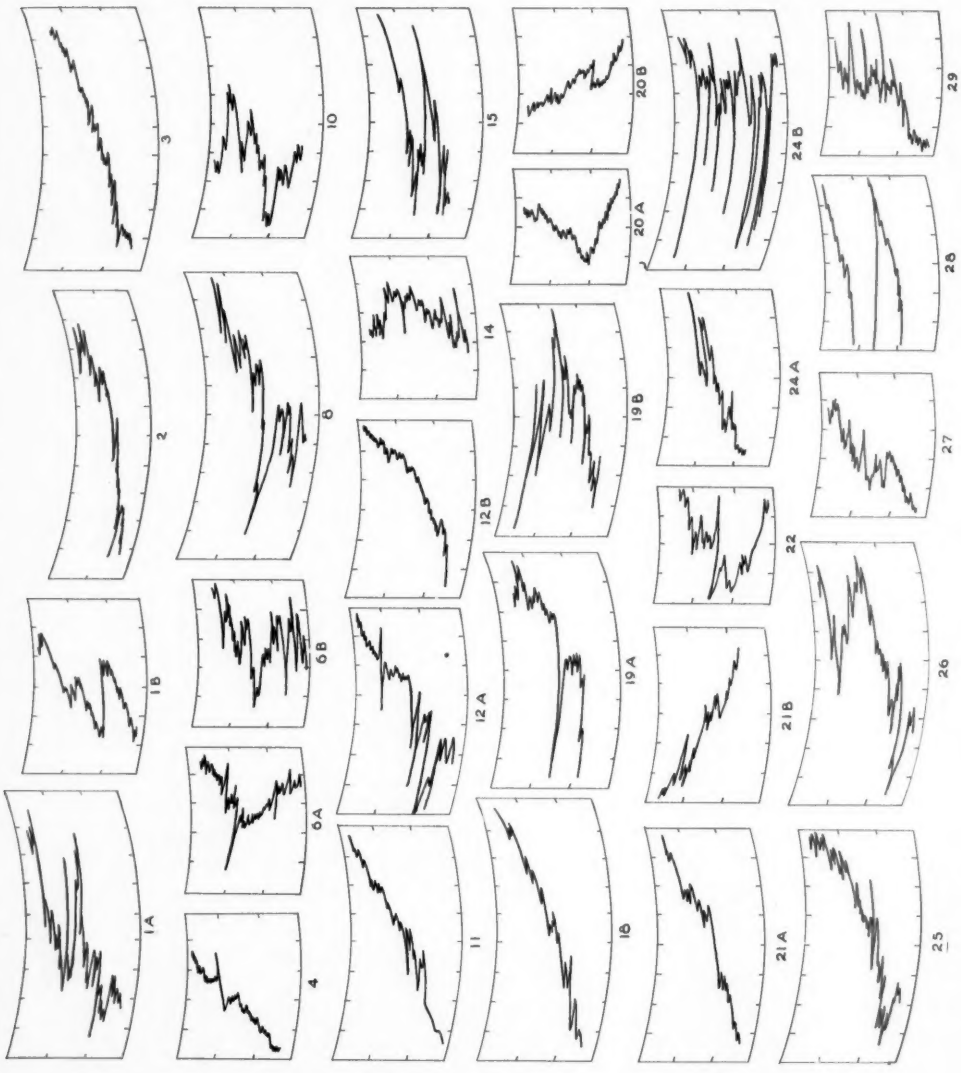

Fig. 1.—Electrometric records of successive days of the menstrual cycle of Case 1. Numbers refer to days of cycle. Duplicate days of other cycles bear letters. Note especially activity at beginning and end of cycle.

the character of the curve is similar on corresponding days. It should be noted that during the first day of the cycle, there was considerable activity. During the second, third, and fourth days uterine activity was less marked. From the sixth to the tenth day, activity increased to be followed on the eleventh day by a quiet period. The twelfth to the fifteenth days were again active with a quiet

eighteenth day. The nineteenth day was active but the twentieth to the twenty-fourth days showed only a moderate degree of activity. Beginning the twenty-fourth and continuing to the twenty-seventh, activity was more marked and, with the possible exception of the twenty-eighth, this continued until the end of the twenty-ninth day. These studies indicate that uterine activity is not a constant finding throughout the cycle nor is it confined to any part of the cycle but comes and goes. Information regarding the physiology of the uterus during the entire cycle is too fragmentary to indicate any possible correlations with electrical activity.

TABLE I. A TOTAL OF 56 RECORDINGS WERE MADE ON 17 PATIENTS

Total number of patients, 17; and total number of observations, 56

PATIENTS	AGE	TYPE OF CASES OR STATUS OF PATIENT
1. R.F.	27	Daily observations of a complete menstrual cycle
2. N.H.	26	Dysmenorrhea beginning 7 days premenstrual. Tenth day of cycle. Suspension of uterus 6 mo. prior to recording
3.	30	Seventeenth day of cycle
4. M.S.	32	Eighth day of cycle. Left ectopic 2½ yr. ago
5.	53	2 yr. postmenopause
6.	65	23 yr. postmenopause. Patient receiving ovarian hormone, record similar to Case 6
7.	17	Seventeenth, eighteenth and nineteenth day postmenses
8.	19	3 days post dilatation and curettage
9. D.G.	17	6 days postmenses. Observations before and after 1 c.c. of ergotrate, given intravenously
10.	21	18 days postmenses, observations before and after ergotrate
11.	17	22 days postmenses, observations before and after pituitrin
12.	28	8 days postmenses, observations before and after pituitrin
13.	24	11 days postmenses, observations before and after pituitrin
14. S.H.	46	Menopause syndrome, menses irregular and scanty, given 10,000 R.U. of estradiol benzoate and observations made 24 hours later
15. C.M.	45	Menorrhagia of menopause, 2 days post dilatation and curettage
16. H.G.	49	Spontaneous menopause 1 yr. Has had 2 menstrual periods in past yr. Received 20,000 I.U. ovarian hormone in past two weeks
17.	27	Fifteenth day postmenses, normal periods

There were no similar potential changes recorded with the application of both electrodes to the anterior lips of the cervix or on attaching one electrode to the cervix and one to the vaginal mucous membrane.

b. *Menopause Cases.*—As a control for this group of determinations, recordings were taken from a number of cases of menopause. Some of these graphs are charted in Fig. 2. A brief sample from a forty-six-year-old menopausal patient is shown in Fig. 2, *A*. This obviously is a quiet uterus. In Fig. 2, *B* is the record of a 53-year-old patient with flushes and headaches two years after the onset of menopause. This record seems to be quite characteristic of active uterine contractions. In Fig. 2, *C* is recorded a case of menorrhagia of menopause two days after a dilatation and curettage. This is obviously a relatively inactive uterus. In Fig. 2, *D* is shown the records of a patient with spontaneous menopause of one year's duration who had received over twenty thousand international units of ovarian hormone in the last two weeks. This record points to the possibility that the administration of ovarian hormone has increased uterine activity.

c. *Effect of Drugs.*—The effect of other drugs on the uterus is shown in Fig. 3. In Fig. 3, *A* is a record taken from a 17-year-old patient six days postmenses. This is obviously a moderately active uterus. At the beginning of the record in Fig. 3, *A'*, 1 c.c. of ergotrate was given intravenously. The following fifteen minutes of record show a very marked increase in the electrical activity. In Fig. 3, *B* a similar record from a 21-year-old patient, eighteen days postmenses is shown. One cubic centimeter of ergotrate was introduced intravenously at the point marked with the arrow and thirty minutes later as shown in Fig. 3, *B'*, electrical

activity has increased considerably and cramps reported as indicated by the arrow. In Fig. 3, *C* is a record from a 24-year-old patient, eleven days postmenses. The records show a moderately quiet uterus. Fifteen minutes after the injection of ½ c.c. of pituitrin, the record shown in Fig. 3, *C'* gives evidence of a considerable increase in uterine activity.

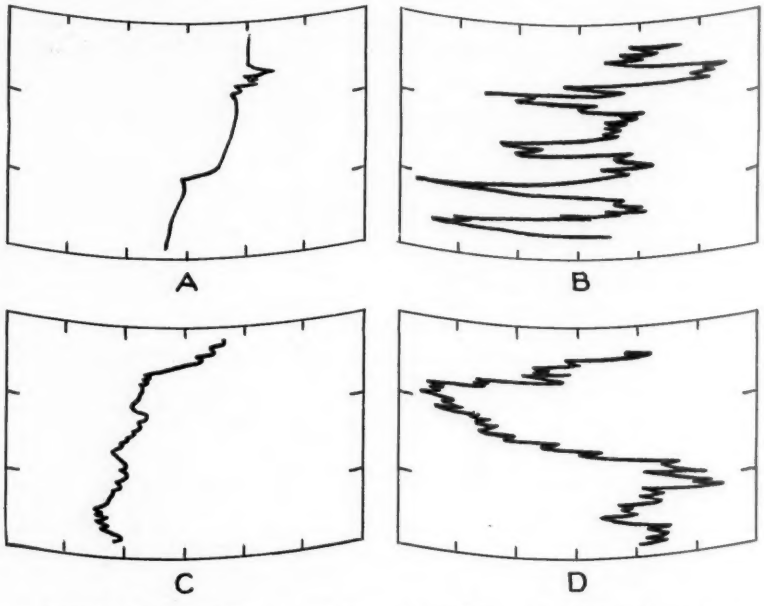

Fig. 2.—Records of menopause. *A*, 46-year-old patient; *B*, 53-year-old patient, with flushes and headaches; *C*, menorrhagia; and *D*, 49-year-old patient, with estrone.

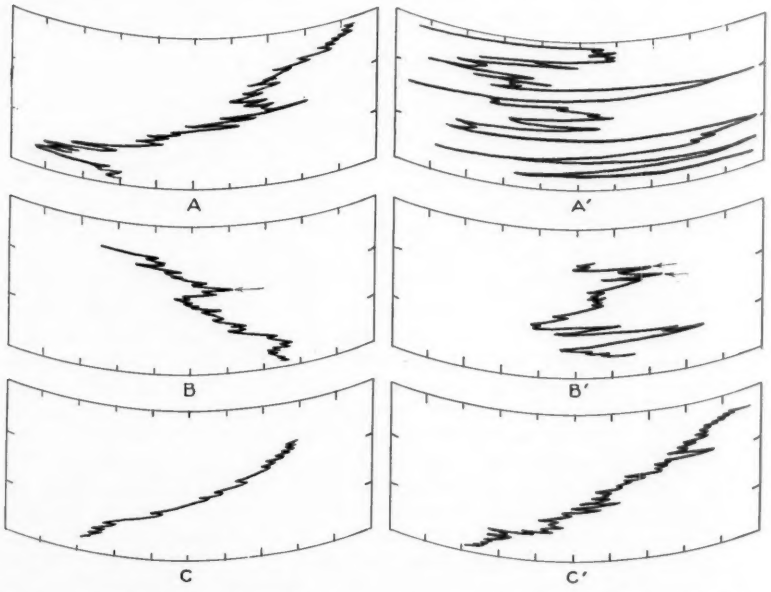

Fig. 3.—Records of young patients. *A*, 17-year-old patient, before ergotrate; *A'*, 17-year-old patient, after ergotrate. *B*, 21-year-old patient, before ergotrate; *B'*, 21-year-old patient, after ergotrate. *C*, 24-year-old patient, before pituitrin; *C'*, 24-year-old patient, after pituitrin.

The effect of 10,000 rat units of estradiol benzoate is shown in Fig. 4 with records taken from a 46-year-old patient, showing the menopause syndrome with irregular and scanty menses. In Fig. 4, *A* is a record taken at the time of administration of the hormone as indicated by the arrow. In the succeeding hour, no essential change in the record occurred, the electrometric records being characterized by relatively little uterine activity. Twenty-four hours later the record showed a marked change. In Fig. 4, *B* the first five minutes of the record taken at slow speed shows a very great increase in electrical activity. In the upper part of the figure this activity was resolved by increasing the speed of the paper to six inches per minute. It will be noted in the portion marked "fast" that the electrical record shows wide swings at relatively high frequency. During this period, the patient complained of cramps.

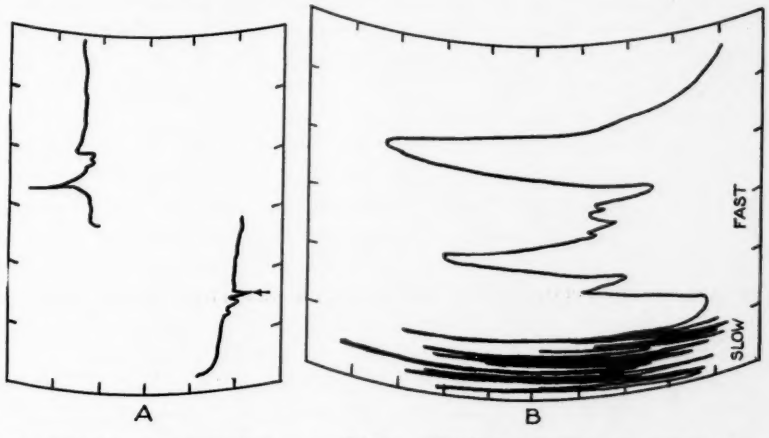

Fig. 4.—Records of menopause. *A*, Before estradiol benzoate at arrow; *B*, after estradiol benzoate.

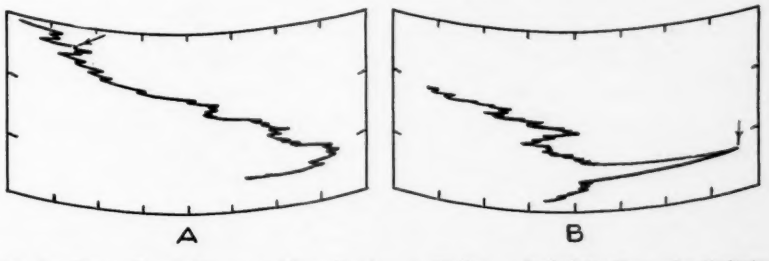

Fig. 5.—Records of 28-year-old patient. *A*, Before administration of pituitrin, at arrow; *B*, twenty-five minutes after, showing wide swing with report of cramp, at arrow.

The correlation of sharp increases in potential difference with cramps had been noted in Case 1, in which dysmenorrhea was present. A reference to Fig. 1 will also show that on the first day of the cycle, and during the last five days of the cycle, there were wide voltage swings. At the time of their occurrence the patient reported a cramp. In fact, it was possible to predict the onset of a cramp by watching the electrical record before the patient reported it. As a further check on this, three patients were studied at varying times in the cycle following the administration of pituitrin. In Fig. 5 a record is shown from a 28-year-old patient eight days after menses. This record shows in Fig. 5, *A* that the uterus is fairly quiet until the administration of 0.5 c.c. of pituitrin, as indicated by the arrow. In Fig. 5, *B*, twenty-five minutes later, is shown a fragment of a record which included a wide swing and a report of cramps at the point marked with the arrow. Finally, it must be recorded that in Case 1, a patient suffering from

dysmenorrhea, the administration of progesterone beginning on or about the twentieth day of the cycle, markedly reduced, if it did not entirely obliterate, cramps. A further study with more exact techniques will be required to elucidate more certainly the relationships between electrical activity of the uterus and cramps.

DISCUSSION

Evidence that the intact human uterus produces direct current characteristics is presented. The potential differences are not chaotic, but produce patterns which are characteristic of uterine motility. Furthermore, the normal spontaneous activity of the uterus, interpreted as contractility, can be recorded with sufficiently constant characteristics to make it possible to state that spontaneous contractions occur in the uterus throughout the entire menstrual cycle, but that deviations from this characteristic pattern can be recognized.

The marked exaggeration of contractions in a patient with spontaneous cramps is comparable to the effect following injections of pituitrin or ergotrate which produce cramps and greatly increased uterine activity, as was shown by the recordings. The decrease in uterine motility and relief from cramps, following the administration of progesterone, indicates a direct effect on uterine contractility and may be attributed to changes in the character of the contractions. If electrical correlates of dysmenorrhea, recorded as increased motility in the uterus, can be further established, then perhaps a criterion for the selection for those patients capable of being relieved of premenstrual pain may be available. The bio-electric findings confirm and may shed some light on the statement of Sevringhaus[15] that certain types of functional dysmenorrhea are favorably influenced by the injection of progesterone, but the mechanism by which the effect is obtained is little understood at the present time. Further studies of the relationships between uterine hypermotility and dysmenorrhea by means of electrical recording is indicated, since Falls and others[16] have shown that the introduction of a hydrostatic bag into the uterus of a seventh-day parturient patient recorded a decrease in uterine tone and motility, following the injection of progesterone.

The increased activity of the uterus to injections of pituitrin occurring in a constant and repetitive character throughout all phases of the cycle, confirms the findings of Kurzrok and others,[3] and Morse and Rubin.[17] The effects as recorded are significant, appearing within fifteen minutes after the injection, and producing severe uterine cramps which coincided with wide voltage swings. Ergotrate caused a more intense and increased motility of the uterus and more severe cramps, the response occurring four to five minutes after intravenous injections.

The response of the uterus during spontaneous menopause to estradiol benzoate suggests the action of the ovaries on uterine motility. The increased activity resulting from estradiol injections within thirty minutes following administration of the hormone indicates that it is absorbed with comparative rapidity. The effect of estradiol on the myometrium is one of stimulation, since an increased uterine contractility was noted in all the patients receiving this hormone.

It is not possible on the basis of the present experiments to explain the action of the sex hormones on the uterus. The technique described

above offers a possible means of analyzing the relationships between uterine physiology and both hormones and other chemical agents. The results obtained indicate a specific hormonal and chemical effect upon the uterine musculature of the cervix.

CONCLUSION

The studies here reported show that records of the slowly changing standing potential between the dorsal and ventral lips of the human cervix can be correlated with phasic changes during menstruation and with administration of sex hormones and other chemical agents. Moreover, the procedure is relatively simple, can be carried out on the intact organism, and introduces a minimum of disturbance to the physiology of the patient.

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Mahoney, J. P., and Chamberlain, John W.: Hydrometrocolpos in Infancy, J. Pediat. **17:** 772, 1940.

This paper deals specifically with a condition infrequently seen in infants, namely the accumulation of abnormally free secretion of fluid above an atretic occlusion in the vagina. The resulting palpable, perhaps visible, abdominal tumor can be identified before operation by a procedure suggested by the writers.

On the basis of four personally observed cases, described in detail, and of a study of the literature, the writers are able to draw several noteworthy conclusions. The obstruction may be due to an imperforate hymen but probably usually is due to arrested development and failure of perforation of the vagina analogous to imperforate anus. Hematocolpos, with symptoms starting only after puberty, suggests that the chief factor in causing discomfort in hydrometrocolpos is the accumulation of thin, mucinous, cloudy fluid, chiefly in the uterus. A simple procedure allows early correct diagnosis. If in the presence of a palpable tumor in lower abdomen of an infant a cystic bulge is palpable in the vagina, a needle puncture is made, and after aspiration of turbid fluid, approximately 20 c.c. of diodrast are injected. Thus can be ruled out other types of tumors requiring laparotomy. Some of the presenting symptoms might be due to compression or obstruction in either urinary or intestinal tract.

Hugo Ehrenfest.

BACTERIOLOGIC CHARACTERISTICS OF ANAEROBIC STREPTOCOCCI RECOVERED FROM POST-PARTUM PATIENTS*

With Special Reference to the Initiation of Infection by These Organisms

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WE HAVE been studying anaerobic streptococci for the past three and one-half years at New York University and Bellevue Hospital, our interest primarily being centered on the fact that we, in common with many other observers, have noted that this organism is frequently responsible for puerperal infection. Time does not permit a lengthy historic review of the bacteriologic work performed heretofore in an attempt to learn and evaluate certain of the characteristics of the organism. Suffice it to say that classification of this streptococcus has been attempted on morphologic characteristics, coupled with certain demonstrable alterations on the substrate in which it is cultured and that the consensus of opinion seems to be that it is nonpathogenic for laboratory animals despite its undoubted human pathogenicity.

We proceeded with the work on the anaerobic streptococcus from two hypothetical possibilities. The first of these assumed that a specific type or group of the organisms, having certain recognizable characteristics, was responsible for the human infections because of some particular attribute of virulence not possessed by the majority. This was a logical assumption, since anaerobic streptococci can be isolated from a large percentage of puerperal women, only a small fraction of whom develop infection. The second possibility assumed that most individuals were refractory to infection with the organism and that only a few exhibited specific susceptibility which might be demonstrable by experimental methods.

The first of these possibilities involved the initial classification of the organisms on an arbitrary basis on the chance that strains which had been shown to have caused infection would fall into groups distinct from nonpathogenic strains and consequently attempted classification on morphologic and biochemical reactions was the first line of investigation.

As a result of our investigations, the following facts were noted:

On horse blood agar after forty-eight hours' incubation in the Brown anaerobic jar all strains of anaerobic streptococci have a superficial resemblance. The colo-

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nies are small, round, slightly convex, and grayish white in color. On this medium, there is produced a peculiar and characteristic sweetish foul odor. In no case was hemolysis noted either immediately or after ninety-six hours, but after storage in the refrigerator for a period of months small zones of hemolysis could be seen surrounding each colony of a few of the strains. Hemolysis, however, did not occur within ninety-six hours on subculture of these colonies.

In cooked meat medium under vaseline the organisms required forty-eight hours for good growth at the end of which time they were seen to have grown best around the meat in the bottom of the tube.

All strains with the exception of four were obligate anaerobes and could not be adapted to growth under aerobic conditions. Four strains after six to eight months' artificial cultivation exhibited tolerance to aerobiosis and grew well on horse blood agar (Table I). Seven of 26 strains produced gas and 15 of the 26 strains produced a very foul, putrid odor (Table II).

TABLE I. COLONY DESCRIPTION

ROUND, CONVEX, TRANSLUCENT, GLOSSY, GRAYISH WHITE STRAINS	ROUND, SLIGHTLY CONVEX, TRANSLUCENT, LIGHTER AT EDGES, DULL, GRAYISH WHITE STRAINS	ROUND, PUNCTIFORM, TRANSPARENT, EFFUSE, GRAY STRAINS
Hod	Odu	Mur
Gow	Odo	Hub
Cob	TerA	Kud
Syl II	TerB	Syl
Tam*	Kas	
Dre	Ase	
Fer	Dau	
Def	Eff	
Mik	Lin	
Rze*		
Myi*		
Myt		
Len*		
13	9	4

*Indicates strains which later exhibited tolerance to aerobic conditions.

TABLE II. GAS AND ODOR PRODUCTION 96 HOUR INCUBATION

FOUL ODOR ALONE	GAS ALONE	GAS AND FOUL ODOR	NO GAS OR ODOR
Hub	Mik	Odu	Mur
Hod	Def	Cob	Syl II
TerA		Syl	Gow
TerB		Dau	Eff
Myi		Kud	Lin
Ase			Rze
Kas			Fer
Myt			Odo
Tam			Dre
Len			
10	2	5	9

Microscopically the organisms appeared as small cocci in chains of three to eight elements. The individual elements were somewhat smaller than staphylococci or hemolytic streptococci. In occasional cultures, more especially in older cultures, diphtheroid forms could be noted. The Gram reaction was variable, and while most of the organisms when freshly cultured were gram-positive, gram-negative forms were not at all uncommon.

It was immediately apparent that morphologic differences were not sufficiently marked to make identification simple, and further, that organisms isolated from human infections did not fall into a specific

group on morphologic criteria. This being the case, further investigation of 26 strains was undertaken as to the properties of the organisms in respect to: (1) the fermentation of various sugars; (2) the quantity of acid produced in media containing sugar; (3) the inhibitory effect of bile; and (4) the ability to hydrolyze sodium hippurate. The results of these studies, each of which was repeated many times, are summarized in Table III.

It will be seen by reference to Table III that clear-cut groupings may be made according to one or another of the criteria employed, but it is also apparent that there is no correlation between grouping by any two of these criteria. The table itself, arranged arbitrarily on the basis of the inhibitory effect of bile, shows three groups of anaerobic streptococci, differing with respect to this inhibition, but these groupings show no uniformity of response to any of the other biochemical tests employed.

Because classification along morphologic and biochemical lines was manifestly unsatisfactory, we determined to attempt to demonstrate more fundamental differences which might exist, by means of serologic technique. It was found possible by inoculation of rabbits with killed cultures, to prepare sera with a moderately high precipitin titer against the strain employed. Twenty-four sera thus prepared were tested against hydrochloric acid extracts of each of the strains with the results which are presented in Table IV. The numbers represent the sum of an arbitrary approximation of the strength of the reaction in three dilutions of extract.

Reference to Table IV shows that in the group of organisms investigated there are many which cross-react, indicating that these organisms possess at least one antigen in common with the organisms used to produce the antiserum. Without going into the immunologic implications too deeply, it has been demonstrated that there are several antigens in the anaerobic streptococcus, one of which might be called type specific, whereas others indicate broader group relationships. It may be possible with further refinement of immunologic technique to classify the anaerobic streptococci according to their antigenic structure. At the same time it becomes increasingly clear that while such a classification may be possible, its practical value is open to question since, with the work already done, no cross-reactions are found to exist among those organisms which have been shown conclusively to be responsible for disease in human beings. Thus four strains isolated in pure culture from the blood of patients exhibiting the typical clinical picture of anaerobic streptococcal septicemia failed to exhibit any immunologic relationships.

It has been demonstrated that there is a relationship of certain strains of anaerobic streptococci to beta hemolytic streptococci of Groups A, B, and C. This relationship was found to exist in 14 of 24 strains tested but no comment in reference to its significance can be made at this time. The greatest number of cross-reactions were noted with Group C hemolytic streptococci, 8 of the 14 strains reacting with sera against this organism.

TABLE III

STRAIN	FINAL PH IN GLUCOSE	GROWTH IN BILE*		FERMENTATION OF		HYDROLYSIS OF SOD. HIPPURATE	FERMENTATION OF†					
		10 PER CENT	40 PER CENT	TREHALOSE	SORBITOL		GLUCO.	MALTO.	LACT.	INUL.	MAN.	SAL.
Syl	4.90	+++	+++	–	–	+	A	A	A	A	–	–
Tam	4.95	++++	++++	–	–	–	A	A	(A)	(A)	–	–
Eff	6.90	++++	++++	–	–	+	A	–	–	A	–	A
Hub	6.22	+++	+	–	–	+	–	–	–	–	–	–
Lin	6.71	+++	+	–	–	+	–	–	–	–	–	A
Kas	7.01	++++	±	–	–	+	–	–	–	–	–	–
Gow	6.69	+++	±	–	–	+	–	–	–	–	–	–
Dau	6.89	+++	±	–	–	+	–	–	–	–	–	–
Mik	4.95	++	±	–	–	–	(A)	–	–	–	(–)	–
Mur	6.83	++	±	–	–	+	–	–	–	–	–	–
Syl II	6.95	++	±	–	–	+	A	–	–	–	–	A
Odo	6.25	++++	±	–	–	+	–	–	–	–	–	–
Hod	6.82	++++	±	–	–	+	A	–	–	–	–	–
Ase	7.10	++++	–	–	–	+	–	–	–	–	–	–
Rze	6.05	+++	–	–	–	+	A	–	–	–	–	–
Len	5.10	++	–	–	–	+	A	A	(–)	(–)	–	–
Fer		+++	–	–	–	+	–	A	–	–	–	A
Myt	7.19	±	–	–	–	–	–	–	–	–	–	–
Odu	6.10	±	–	–	–	+	–	A	–	–	–	–
Myi	5.60	±	–	–	–	+	A	A	A	–	–	A
TerA	6.69	–	–	–	–	+	–	–	–	–	–	–
TerB	6.36	–	–	–	–	+	–	–	–	–	–	–
Kud	7.16	–	–	–	–	–	–	–	–	–	–	–
Dre	7.20	–	–	–	–	–	–	–	–	–	–	–
Def	7.49	–	–	–	–	–	(–)	(–)	(–)	(–)	(–)	(–)
Cob	5.50	–	–	–	–	+	(–)	(–)	(–)	(–)	(–)	(–)

*++++ to – indicates degrees of growth.
†A, acid; (A), acid and gas; – no fermentation; (–) gas but no acid.

TABLE IV. CONDENSED RESULTS OF PRECIPITIN REACTIONS

EXTRACT	SERUM																															
	SYL	TAM	EFF	HUB	LIN	KAS	GOW	DAU	MUR	SYL II	ODO	HOD	ASE	RZE	LEN	FER	MYT	ODU	MYI	TERA	TERB	KUD	DRE	MIK								
Syl	12	0	6	2	2	0	0	0	2	4	1	0	0	3	0	0	0	0	0	1	3	0	0	0								
Tam	0	11	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0								
Eff	0	0	12	0	11	0	0	0	0	6	1	0	0	8	0	1	0	0	0	6	9	0	0	0								
Hub	6	0	2	10	0	0	0	0	0	8	1	0	0	8	0	6	2	0	0	0	0	0	2	0								
Lin	0	0	11	0	10	0	0	0	10	1	2	0	0	6	0	12	0	0	0	9	9	1	2	0								
Kas	0	0	1	0	0	11	0	4	0	1	2	0	3	0	0	0	0	0	0	0	0	0	2	0								
Gow	0	0	11	0	0	0	11	0	3	6	1	0	0	2	0	4	0	0	0	5	4	3	7	0								
Dau	0	0	0	0	0	0	0	12	3	0	1	0	0	1	0	6	0	0	0	0	0	0	0	0								
Mur	0	0	12	0	12	0	0	0	5	6	1	0	0	11	0	0	0	0	0	11	11	0	3	0								
Syl II	0	0	3	0	2	0	0	0	8	8	2	0	0	1	0	0	0	0	0	2	2	0	3	0								
Odo	0	3	0	0	1	0	5	1	0	0	11	0	0	1	0	0	0	0	0	3	6	0	0	0								
Hod	0	0	0	0	0	0	0	0	0	0	4	11	6	0	0	6	0	0	0	0	0	0	0	0								
Ase	0	0	0	0	0	0	0	0	0	0	4	0	10	0	0	0	0	0	0	4	10	2	4	1								
Rze	0	0	0	0	0	0	2	0	0	1	0	0	0	8	0	0	0	0	0	0	0	0	0	0								
Len	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0	0	4	10	0	2	0								
Fer	0	0	9	0	0	0	3	0	9	0	0	0	0	0	0	4	3	0	0	0	0	0	0	0								
Myt	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	6	11	0	0	6	8	0	0	0								
Odu	0	0	2	0	0	0	0	0	8	6	0	0	0	0	0	0	0	10	0	2	0	0	0	0								
Myi	0	0	0	0	10	0	0	0	0	1	0	0	0	0	0	0	0	0	4	1	3	1	2	6								
TerA	0	1	10	0	5	0	0	0	0	2	2	0	0	0	0	0	0	0	0	1	0	0	0	0								
TerB	0	2	11	0	8	0	0	0	0	5	8	0	0	2	0	0	0	0	0	10	12	0	1	0								
Kud	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	11	12	12	2	0								
Dre	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	12	11	0								
Mik	0	0	2	0	0	0	0	0	1	0	3	0	0	0	0	3	0	0	0	0	0	10	12	0								
																				1	0	3	2	11								

On the whole, the investigation of these organisms from the viewpoint that there exists a uniform group of potential pathogens in a larger group of strict saprophytes, has been disappointing. This being the case, it was decided to investigate the possibility that any of the indigenous strains might incite disease under specific conditions. In such an investigation factors altering resistance and favoring growth of the organisms had to be considered. Early in the study it was found that the normal aerobiosis of tissue favored the rapid destruction and phagocytosis of anaerobic streptococci. In most cases of puerperal infection, one is justified in assuming that necrotic remnants of tissue remain in the uterus following parturition, and it was thought possible that such particles of tissue might well serve as a nidus for the growth and dissemination of anaerobic streptococci. Inoculation of these organisms, however, into the uteri of recently delivered rabbits caused no appreciable ill-effects. However, by inoculating fresh cultures of anaerobic streptococci intratesticularly after ligation of the blood supply to the testis, it was found that organisms could be recovered from the necrotic testis seven to fourteen days after inoculation and, further, that within seven days anaerobic streptococci could be demonstrated in the blood stream. This fact is apparently more interesting than significant, since none of these animals exhibited any signs of illness nor did any of them die. Passage of one strain by intratesticular inoculation through 8 successive guinea pigs failed to heighten its virulence for these animals. Attempts to produce infection in guinea pigs, mice, rats, rabbits, and monkeys by a variety of routes of inoculation likewise met with failure. The addition of mucin, reducing substances, and foreign tissue to cultures of the organisms prior to inoculation into animals had no apparent effect.

The fact that anaerobic streptococci are nonpathogenic for laboratory animals and, indeed, for most human beings is not a newly discovered one. It has been noted by almost all investigators of the problem, and it thus seemed probable or at least possible that some serum factor, lethal for the organisms, was present in the common laboratory animals and perhaps in the majority of human beings. This theory would account for the relatively low incidence of infection even in the face of the high percentage of women harboring the organism in the vagina. Further, it had been shown previously by Colebrook and Hare[1] that anaerobic streptococci die rapidly in serum or blood clot. With these considerations in mind, the investigation of a serum factor influencing resistance seemed a profitable line of endeavor.

The study of these factors of resistance is still in its early stage and consequently it is not proper to draw final conclusions, but a few points may be mentioned. It seems fairly certain that phagocytosis alone does not play a major role, since the serum of normal persons is able to activate white cells to phagocytize the organisms to an extent neither greater nor lesser than the serum from persons suffering from severe anaerobic streptococcal septicemia. One should expect, if lack of phagocytic power alone determined susceptibility, that serum from a patient in the early stages of such an infection would show a reduced activating power, which theoretically at least would increase

when and if recovery ensued. This has not been found to be the case, for we have noted both greater and lesser degrees of phagocytosis for the same organism in what appears to be a wholly erratic manner with no apparent relationship to the stage of the disease. In all fairness, it must be mentioned that the study of the phenomenon of phagocytosis is one beset with many difficulties, owing to this wide variation even in normal subjects from day to day.

The question as to whether or not a bactericidal factor for the anaerobic streptococcus is present in the sera of human beings or animals is another one which has not fully been answered. From the work so far performed, it is a fact that exposure to certain sera for lengths of time varying from twenty-four to forty-eight hours kills the organisms so that subculture of the serum-organism mixture is no longer possible. In one instance recently under our observation, the serum from a patient ill with anaerobic streptococcal septicemia for over forty days, failed to kill a fresh culture of the organisms isolated from the patient's blood stream but did destroy other cultures of anaerobic streptococci serologically unrelated to this organism. In this instance, of course, the evidence points to a specifically virulent strain of the organism rather than to a lack of any nonspecific serum factor. Again, we would like to state that this work is not completed and that, therefore, conclusions are not justified.

It is interesting to note that recovery from anaerobic streptococcal septicemia does not result in the presence of demonstrable antibodies in the patient's serum. In all the cases which have been under study, no precipitins or agglutinins against the organism isolated from the blood stream of the patient could be found even after rather long periods of illness. This was true in spite of the fact that there could be no question as to the specificity of the organism causing the disease, for in many cases it was isolated repeatedly from the blood stream. In a few cases, however, a specific hypersensitivity could be demonstrated late in convalescence by means of skin tests with extracts of the organism recovered from the patient.

It follows from the results described above that the mechanism of infection with the anaerobic streptococcus depends more upon individual patient susceptibility than upon a specific group or type of virulent organism and that recovery proceeds in a manner not completely understood at the present time. Until a greater amount of experimental work is performed, however, no final conclusions are permissible.

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RUPTURED UTERUS

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RUPTURED uterus, although of infrequent occurrence, ranks first among obstetric complications in its disastrous effect upon both mother and baby. The infrequency of its occurrence in itself adds to the seriousness of the situation, because very few obstetricians observe enough cases to become proficient in diagnosis and treatment. Exceedingly important is the fact that the possibility of ruptured uterus must always be kept in mind even though labor and delivery seem to be pursuing a normal course. The case in which the typical textbook set of symptoms and signs occur probably will not often be overlooked. However it is the unusual variation of this distressing obstetric problem which all too frequently is not recognized until precious and irretrievable time has been lost. Diagnosis of all cases must be prompt and treatment instituted immediately and effectively if the appalling death rate of ruptured uterus is ever to be reduced.

This paper presents a survey of a larger group of cases with the object of re-familiarizing both general practitioner and obstetrician with the various features of this infrequent but nevertheless tragic condition.

In an unusually active practice of forty years, DeLee attended 19 patients with complete rupture, 11 of whom died; and 19 patients with incomplete tear, 3 of whom died. At St. Luke's Hospital, Cleveland, there occurred 12 cases of uterine rupture in 17,793 deliveries or an incidence of 1 in 1,483 deliveries, 5 of whom died.

The data herein presented and conclusions arrived at are the result of an analytical survey of 45 cases of ruptured uteri, only 3 of which have been previously reported (Woodward). Twelve of these cases occurred at St. Luke's Hospital. The remaining 33 cases represent the total number of uterine ruptures occurring during the past five years in 41 of the 47 member hospitals of The Hospital Obstetric Society of Ohio.

Each case report is the result of a detailed personal communication with the physician in charge of the case. At this point I wish to express my deep appreciation to those physicians who were kind enough to cooperate with me in this study.

AGE INCIDENCE

In the patients studied, the age span varied from 19 to 48 years, with an average age of 31 years. It is evident that the possibility of uterine rupture must be considered in every gravida regardless of age.

PARITY

The number of pregnancies preceding the one in which rupture occurred varied from none to fifteen.

TABLE I. AGE INCIDENCE

Under 20	2	35 to 40	8
20 to 30	7	40 to 45	5
25 to 30	11	45 to 50	1
30 to 35	11		

TABLE II. PARITY

Parity	0	i	ii	iii	iv	v	vi	vii	viii	xi	xv
Number of cases	2	14	8	4	5	5	1	3	1	1	1

In 2 patients, uterine rupture occurred during the first pregnancy, and in both was the result of trauma caused by internal podalic version. Fourteen patients had only one previous pregnancy and 9 of these were patients in whom previous cesarean section had been performed. Eight patients had two preceding pregnancies, and of these, five had been subjected to a previous section. There were a total of 18 cases in which cesarean section had been performed prior to the pregnancy in which rupture occurred (Table III). It is, therefore, apparent that the most frequent cause of uterine rupture in patients of lesser gravidity is previous cesarean section; whereas spontaneous rupture is the most frequent cause in patients of greater gravidity.

LENGTH OF LABOR

The length of labor preceding the rupture varied considerably, from no labor to 96 hours. In 9 patients rupture occurred before the onset of labor. There were 30 patients with labor of less than ten hours and 15 patients with labor more than ten hours. The average length of labor in the patients where previous section had been performed was nine hours, as compared with eighteen hours of labor in the patients where section had not been performed.

If we exclude all cases occurring before the onset of labor or during the actual delivery, and only include the cases occurring during labor, we find that the average length of labor before rupture is twelve hours.

CAUSE OF UTERINE RUPTURE

Of paramount importance, of course, is the reason why uterine tear occurs. Only by careful consideration of the causative factors involved will we be able to determine in the future how best to avoid rupture of the uterus.

TABLE III. CAUSE OF RUPTURE

	CASES	SURVIVED	DIED
1. Previous cesarean section	18	16	2
2. Cause not definitely determined, perhaps due to myometrial changes	9	3	6
3. Internal podalic version	5	3	2
4. Uncorrected transverse presentation	4	2	2
5. Obstructed labor			
a. Cephalopelvic disproportion	4	1	3
b. Obstructing ovarian cyst	2	1	1
6. Previous pelvic peritonitis	1	1	0
7. Eclamptic convulsion	1	0	1
8. Previous curettage	1	1	0

At this point, we might consider which of these cases possibly could have been prevented. Attendance at each case would be the only accurate way of determining which patient could have been managed more judiciously, so that rupture would not have occurred. However, from the evidence at hand, we can say that most probably the ruptures represented in items 3, 4, and 5, that is 15 cases (33

per cent), could have been prevented by more accurate diagnosis and more efficient treatment of the primary obstetric condition.

Internal podalic version is a very useful maneuver. However great care must be taken in its performance, and it should never be used if any of the well known contraindications are present. Transverse presentation can and must be recognized early if it is to be adequately treated. A more liberal use of the x-ray whenever any doubt exists would bring these cases to light soon enough to institute the proper corrective measures. Also in several of the cases where the indication for the previous cesarean section was cephalopelvic disproportion, the patient should not have been permitted to labor more than a few hours. Whenever a previous section is done for cephalopelvic disproportion, termination of succeeding pregnancies by cesarean section would be the method of choice, unless the baby is much smaller than the previous one. At any rate, if labor is permitted, all preparations should be made to promptly treat a threatened or actual rupture, including readily available blood donors.

ANALYSIS OF RUPTURED UTERI WITH PREVIOUS CESAREAN SECTION

Table IV is a presentation of the salient features occurring in the cases of uterine rupture following previous cesarean section. Of the 45 cases in this entire survey, 18, or 40 per cent, were in patients previously subjected to section. Nine of the sections were performed because of disproportion, 2 each because of placenta previa and ablatio placentae, 3 as treatment for eclampsia, and 1 because of reported interlocked twins.

Two methods of treatment were used, supracervical hysterectomy and suturing of the lacerated uterus. Of the 9 patients treated by hysterectomy, 1 died and 1 had a stormy convalescence; the remainder recovered uneventfully. Of the 8 patients treated by suturing of the uterine tear, all recovered, but one had a stormy convalescence. One patient died before treatment could be instituted; however, death was probably due to a pre-existing pneumonia rather than from the ruptured uterus.

TABLE IV. RUPTURED UTERI FOLLOWING PREVIOUS CESAREAN SECTION

CASE	INDICATION FOR SECTION	LENGTH OF LABOR	TIME OF RUPTURE		TREATMENT	RESULT	
			BEFORE LABOR	DURING LABOR		MOTHER	BABY
1	Disproportion	4 hr.		×	Suture	Survived	Dead
2	Disproportion	52 hr.		×	Suture	Survived	Survived
3	Disproportion	10 hr.		×	Suture	Stormy recovery	Dead
4	Disproportion	36 hr. (6 mo.)		×	Suture	Survived	Dead
5	Disproportion	0 (7 mo.)	×		Hysterectomy	Survived	Dead
6	Disproportion	0	×		Suture	Survived	Dead
7	Disproportion	5 hr.		×	Suture	Survived	Dead
8	Disproportion	1 hr.		×	Hysterectomy	Survived	Survived
9	Disproportion	14 hr.		×	Hysterectomy	Survived	Dead
10	Placenta previa	4 hr.		×	Hysterectomy	Survived	Dead
11	Placenta previa	0	×		Hysterectomy	Survived	Survived
12	Ablatio placentae	0	×		Suture	Survived	Survived
13	Ablatio placentae (cervical section)	18 hr.		×	Suture	Survived	Survived
14	Eclampsia	0	×		Hysterectomy	Stormy recovery	Dead
15	Eclampsia	10 hr.		×	Hysterectomy	Survived	Dead
16	Eclampsia (cervical section)	3 hr.		×	Hysterectomy	Survived	Dead
17	Interlocked twins	3 hr.		×	Hysterectomy	Died	Dead
18	Indication unknown	0	×		No time	Died	Dead

From the foregoing it would seem that the treatment of choice is suture of the torn uterus, although both methods of treatment gave nearly comparable results. In deciding upon which form of treatment to use, several factors must be borne in mind. If the patient has no living children or only one child, it probably would be best to try to preserve the uterus; however, the possibility of rupture must be borne in mind in the event of future pregnancy. If a pregnancy does occur, delivery should be by elective section and tubal sterilization or hysterectomy about two weeks before the estimated date of confinement. Case 3 (Table IV) illustrates this point. This patient had a ruptured uterus in 1936, following a previous cesarean section. Treatment was by suture of the laceration. Then in 1939 the patient again became pregnant, and this time she was delivered by elective section and hysterectomy.

Of the 18 patients having had a previous cesarean section, 6 suffered rupture of the uterus before the onset of labor; while of the 27 nonsection cases, only 3 sustained uterine rupture before labor commenced. Uterine tear is much more likely to occur before the onset of labor in patients subjected to previous cesarean section than in those not having had a previous section.

TABLE V. TIME OF RUPTURE

	ENTIRE SERIES	PREVIOUS SECTION CASES	NONSECTION CASES
Before labor	9	6	3
During labor	26	12	14
During delivery	10	0	10

The dictum "Once a cesarean always a cesarean" even if accepted by all obstetricians would not be sufficient to protect every previously sectioned patient from the hazards of uterine rupture. It is imperative that every gravida with a history of previous section be very closely watched at all times during her pregnancy, and especially during the last two or three months, for evidence of impending or even actual rupture. Complaints of vague abdominal pain and tenderness should not be dismissed without a careful examination and frequent observation. Typing and cross-matching of blood donors should be done not later than the beginning of the third trimester, so that transfusions can be performed without delay if uterine rupture does occur.

The maternal mortality rate in the group of patients having had a previous section was 11 per cent. The fetal mortality rate in this group was 72 per cent. Various other investigators have found the maternal mortality rate to vary from 13 per cent (Asa B. Davis) to 50 per cent (Weber).

The incidence of uterine rupture following classical section varies from 2 per cent (Kerr) to 6 per cent (Audebert). Gelle, in 1932, reviewed all available cases of cervical section and estimated that the incidence of uterine rupture was 0.25 per cent or one-sixteenth of that found following the classical section. The present series includes 2 cases of rupture, following a previous cervical section; both patients recovered uneventfully.

Shock is the most prominent and the most serious manifestation of uterine rupture. However, shock was present in only 2 of the 18 cases where previous section had been done, while it was a prominent symptom in 23 of the 27 nonsection cases. This explains the low mortality rate in the group of previous section cases.

The obstetrician who decides in favor of vaginal delivery in the management of a patient having had a previous section (disproportion not being a factor), assumes less of a maternal risk than if he routinely re-sectioned all patients. The average incidence of uterine tear following previous classical section is about 4 per cent, i.e., 4 patients out of every hundred would suffer uterine rupture if they were all permitted to deliver vaginally. Of these 4, only 11 per cent, or 0.36 patient, would die. Whereas, if the entire hundred patients were routinely re-sectioned, the basic mortality rate would be from 1 to 2 per cent (Skeel and Jordan).

UTERINE RUPTURE OCCURRING DURING DELIVERY

There were 10 cases in which rupture took place during the actual delivery. As we can see (Table VI) internal podalic version was the cause of 60 per cent of the uterine tears in this group, with a mortality rate of 50 per cent.

TABLE VI. TYPE OF DELIVERY

	CASES	SURVIVED	DIED
Internal podalic version	6	3	3
Spontaneous delivery	3	2	1
Breech extraction	1	0	1

LOCATION OF RUPTURE

Table VII shows that laceration of the posterior wall of the uterus was the most disastrous, causing a 100 per cent mortality in this series. Lacerations of the lower uterine segment caused the next highest death rate, 5 of the 9 patients dying. A distinct danger of lower uterine segment rupture is involvement of the bladder. Left lateral ruptures were the next most serious, with a 50 per cent maternal mortality.

TABLE VII. LOCATION OF RUPTURE

	CASES	SURVIVED	DIED
1. Location not stated	2	1	1
2. Previous classical scar	16	14	2
3. Previous cervical section scar	2	2	0
4. Lower uterine segment	9	4	5
5. Posterior wall	4	0	4
6. Left lateral	6	3	3
7. Right lateral	3	2	1
8. Bilateral	1	0	1
9. Anterior wall	2	1	1

TYPE OF RUPTURE

The two recognized types are the complete and incomplete. The incomplete variety is characterized by the fact that the endometrium and myometrium are involved, but the uterine peritoneum remains intact. Whereas, in the complete type, the peritoneum is also lacerated, thus making a direct communication between the interior of the uterus and the general peritoneal cavity. Peritonitis is of more frequent occurrence in the complete type.

In this series there were 38 complete uterine ruptures and 7 incomplete ruptures. There is little doubt that there are probably more incomplete ruptures than are recognized. It is a good idea to explore carefully the interior of every uterus where there has been a difficult instrumental delivery or where internal manipulation has been performed. Internal uterine exploration under aseptic conditions bears very little risk, and certainly far less risk than a neglected incomplete rupture. Table VIII illustrates the greater risk of complete rupture.

TABLE VIII. TYPE OF RUPTURE

	CASES	SURVIVED	DIED
Complete rupture	38	22	16
Incomplete rupture	7	6	1

Of the 22 patients with complete rupture that survived, 6 had a stormy convalescence due to peritonitis. The 6 surviving patients with incomplete rupture recovered uneventfully.

A study of the fate of the infant also reveals the more devastating effect of the complete type of rupture (Table IX).

TABLE IX. TYPE OF RUPTURE

	CASES	SURVIVED	DIED
Complete rupture	38	6	32
Incomplete rupture	7	4	3

METHOD OF TREATMENT IN CASES WHERE PREVIOUS SECTION HAD NOT BEEN PERFORMED

A study of Table X reveals that the 7 patients in the first group died of hemorrhage and shock before effective treatment could be instituted. However, in several of these cases, the diagnosis was not made until it was too late. Earlier diagnosis might have saved these patients.

Supracervical hysterectomy gave the best results. Most of the uteri were lacerated in such a manner that removal of the uterus was the only feasible method of treatment. Two patients were treated by suturing of the laceration; one patient died of paralytic ileus and the other died of peritonitis which apparently was present at the time the laparotomy was done.

TABLE X. TREATMENT OF NONSECTIONED RUPTURED UTERI

	CASES	RECOVERED	DIED
1. No time for treatment	7	0	7
2. Supracervical hysterectomy	17	12	5
3. Laceration sutured	2	0	2
4. Uterine arteries clamped vaginally	1	0	1

IMMEDIATE CAUSE OF DEATH

By far the most frequent immediate cause of death was hemorrhage and shock. Most of these patients bled so profusely intra-abdominally that death occurred before treatment could be instituted, or, if operation was performed, death occurred soon afterward.

Nine patients died before laparotomy could be performed. Of these, in only one case was there time for a blood transfusion. Five patients died during or shortly after operation. Three of these had transfusion.

Nineteen of the 28 surviving patients had from 1 to 7 transfusions.

MORTALITY

In this series of 45 cases, there were 17 maternal deaths and 31 fetal deaths, that is, a death rate of 37 per cent and 69 per cent, respectively.

TABLE XII. MORTALITY RATE

	NUMBER OF CASES	MATERNAL DEATHS	FETAL DEATHS
Entire series	45	17 (37%)	31 (69%)
Previous section cases	18	2 (11%)	13 (72%)
Nonsection cases	27	15 (55%)	18 (66%)

The death rate occurring in the present series compares favorably with that of other recent investigators. Asa B. Davis, in 1927, had a total maternal death rate of 56.6 per cent, and a previous section mortality rate of 12.5 per cent. McNeile and McBurney, in 1935, had a maternal death rate of 20 per cent in previous section cases and 90 per cent in nonsection cases. Davis found a fetal death rate of 80 per cent in section and nonsection cases alike.

SUMMARY

1. An analytical survey of 45 cases of uterine rupture is herein presented.

2. The most frequent cause of rupture of the uterus was previous cesarean section. The trauma of internal podalic version and uncorrected transverse presentation also were prominent causative factors.

3. Supracervical hysterectomy or suture of the uterine laceration gave equally good results in the treatment of cases where rupture followed a previous cesarean section.

4. Supracervical hysterectomy was the treatment of choice in the nonsection cases of uterine rupture.

5. There is a definite danger of uterine rupture before the onset of labor, particularly in patients where previous cesarean section had been performed.

6. Internal podalic version was responsible for 60 per cent of the uterine ruptures occurring during the time of delivery.

7. Complete rupture of the uterus is far more serious than the incomplete variety.

8. Hemorrhage and shock was the most common immediate cause of death.

9. The maternal mortality rate for the entire series was 37 per cent; total fetal mortality rate was 69 per cent.

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TREATMENT OF MENSTRUAL DISORDERS WITH PREGNANT MARES' SERUM

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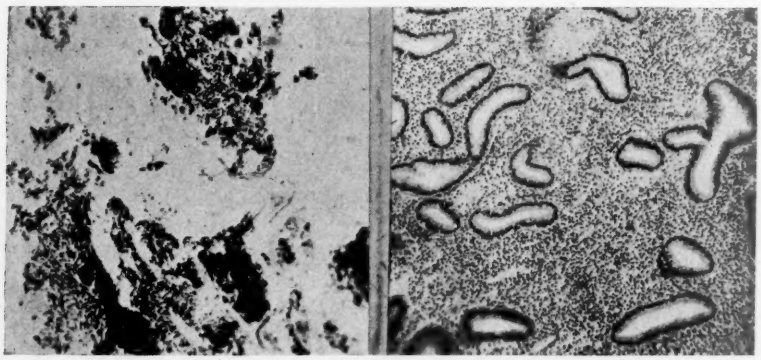
PREGNANT mares' serum was shown by Cole and Hart[1] to possess a powerful stimulating effect on the ovaries of the immature rat, producing ovulation and corpus luteum formation. Evans[2] and Reichert,[3] in their studies on hypophysectomized rats, showed the contrast between pregnant mares' serum and chorionic gonadotropin: The pregnant mares' serum is effective in bringing about structural restoration of the female reproductive system, and chorionic gonadotropin is not. Also, pregnant mares' serum is not excreted by the kidney; therefore, the total dose is available for stimulation. Clinical studies on pregnant mares' serum by Bowes[4] and Frank,[5] Davis and Koff,[6] Dodds and his associates,[7] and Kurzrok,[8] gave indifferent or inconclusive results.

While interest in this hormone centered mostly about its use in overcoming sterility, it has been used in all forms of menstrual disturbances with varying success.[9-13]

Because of these conflicting reports, further clinical experiences with this hormone are here recorded. Seventeen patients with menstrual disturbances were treated: 13 suffered from amenorrhea or oligomenorrhea, and 4 had menorrhagia or metromenorrhagia. In 12 of the 17 patients endometrial biopsies were performed with a suction curette and 4 of the remaining 5 were followed with vaginal smears.



A. *B.*

Fig. 1.—*A*, Endometrial biopsy showing atrophy in patient (H. N.) with amenorrhea of ten months' duration. *B*, Proliferative phase after 3,000 international units of gonadin. Regular monthly periods have occurred for eight months after treatment discontinued. (×125.)

A. *B.*

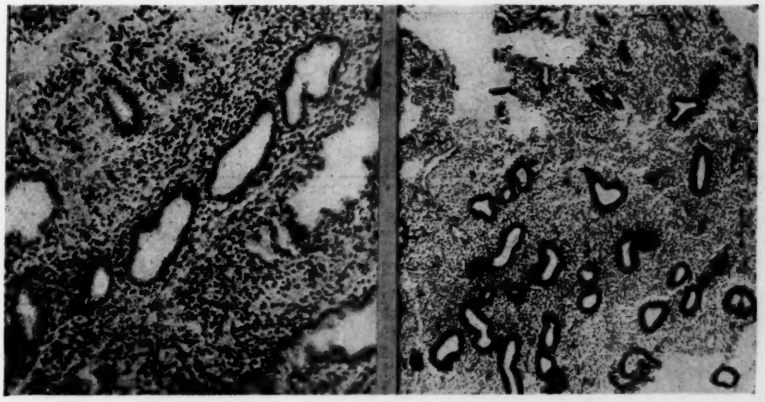
Fig. 2.—*A*, Endometrial biopsy showing Cullen's hyperplasia in patient (H. M.) with menorrhagia after three weeks' flow. *B*, Proliferative phase after 3,000 international units of gonadin. Regular three- to seven-day periods have occurred for eight months. (×125.)

Following the suggestion of Novak, patients with amenorrhea and hypomenorrhea were primed with estrone, 16,000 units being the usual preliminary dosage. All of the patients were given a careful physical, endocrinologic and gynecologic examination before pregnant mares' serum was given. All other medication was discontinued. The plan of treatment was to administer 200 international units of pregnant mares'

serum* intramuscularly, every other day, until 15 injections or 3,000 international units were administered. A rest period followed the injections and, if there was no clinical response, the course was repeated. At intervals, depending upon the progress of the individual patient, endometrial biopsies were again taken. Results of treatment are shown in Table I.

DISCUSSION

Seven of the 17 patients with amenorrhea and oligomenorrhea were affected by treatment during the period of injections. When these patients were interviewed eight months later, 2 of the 7 had more than temporary benefit, and in a third patient (A. R.), the four- to six-month menstrual interval was reduced to an interval of three months. Of significant interest is the case of R. Z., aged 17 years, the only case of primary amenorrhea in the series, who failed to show any immediate clinical benefit from treatment, and whose endometrial biopsies showed atrophy before and after treatment. One month after the injections were discontinued she



A. *B.*

Fig. 3.—*A*, Endometrial biopsy showing secretory phase in patient (P. M.) with menorrhagia after nine weeks' flow. *B*, Proliferative phase after 4,200 international units of gonadin. Normal menses occurred for four months; then menorrhagia recurred. (×125.)

menstruated and has continued to have regular monthly periods after eight months. Of further interest is the patient (J. H.) who had acromegaly with an enlarged sella turcica. Since there has been speculation that amenorrhea in acromegaly is the result of suppressed hormone secretion from intrasellar pressure, improvement might have been anticipated from substitutional pituitary therapy.

All four patients with menorrhagia were improved at the time the injections were administered. One of these (H. A.), who had been married for five years without conceiving, became pregnant during the course of treatment. This might be interpreted as an example of induced ovulation, although there was no proof that she was not ovulating prior to treatment. Of the remaining 3 cases of menorrhagia, 2 (H. M. and V. B.) have continued to be benefited eight months after treatment was discontinued.

Three of the 8 patients with amenorrhea and oligomenorrhea, in whom endometrial biopsies were taken, showed changes from an atrophic to a proliferative phase, while no change from the original atrophic pattern was discernible in 4 others. Vaginal smears, in the 3 cases in which they were carefully studied, showed no definite change following the injections. The endometrial picture in the 3 patients with menorrhagia before and after treatment, indicated a regression from the original pattern of hyperplasia to one of proliferation. These changes would seem rather significant in view of the clinical course of these patients.

*Acknowledgment is made to Mr. Donald Wonder of Cutter Laboratories for a generous supply of gonadin used in these studies.

TABLE I. RÉSUMÉ OF CASES TREATED WITH PREGNANT MARES' SERUM (P. M. S.)

	NAME AGE	MENSTRUAL HISTORY	PREVIOUS TREATMENT	AMOUNT P.M.S.	CLINICAL RESULTS		ENDOMETRIUM		VAGINAL SMEARS	
					IMMEDIATE	AFTER 8 MONTHS	BEFORE	AFTER	BEFORE	AFTER
Hypomenorrhea and	A. B. 29	30-day interval. Scant flow	None	6,000 I.U.	0	0	Atrophy	Atrophy	---	---
	R. Z. 17	Primary amenorrhea	Massive doses of estrone	6,000 I.U.	0	Regular periods began 1 mo. after treatment	Atrophy	Atrophy	---	---
	L. M. 27	Interval of 6 mo.; varying periods of menorrhagia and metrorrhagia	Series of estrone and progestin	6,000 I.U.	2 periods at 30-day interval	No further period	Atrophy	Atrophy	---	---
	J. H. 32	Sudden cessation 3 yr. previous	None	6,000 I.U.	0	0	Atrophy	Atrophy	---	---
	C. P. 27	Interval 3-6 mo. 1 day duration past 10 yr.	None	4,200 I.U.	Menstruated	Regular monthly periods	Proliferation	Proliferation	---	---
	M. S. 17	Irreg., 3-6 periods a yr. Last menstrual period 3 mo. previous	Desiccated thyroid	6,000 I.U.	Menses more regular during treatment	About same as formerly	Atrophy	Proliferation	---	---
	H. N. 20	Irreg. interval 2-3 mo. Last menstrual period 10 mo. previous	None	3,000 I.U.	Menstruated	Regular monthly periods	Atrophy	Proliferation	---	---
	M. O. 22	Interval 6 wk. in 4 mo. Scant flow	None	5,400 I.U.	Menses more regular during treatment	Not heard from	Atrophy	Proliferation	---	---

Amenorrhea	A. R. 18	Interval 4 to 6 mo. Scant flow	None	3,000 I.U.	Menstruated	Regular for 4 mo. No period since	Atrophy	---	---	---
	M. A. 20	Fairly regular until last menstrual period 12 mo. previous	Estrone for 9 mo. period	4,800 I.U.	Vaginal bleeding one time	0	---	---	Neg.	Pos.
	P. B. 25	Always irregular. Last menstrual period 15 mo. previous	Thyroid; estrone; gonadotropic hormone; urinary gonadotropin	1,500 I.U.	0	0	---	---	---	---
	L. R. 30	Scant flow. Last menstrual period 10 yr. previous	Estrone, two long series	6,000 I.U.	0	0	---	---	Weak Pos.	Neg.
	M. P. 33	Irregular past 2 yr. Last menstrual period 3 mo. previous	Estrone	3,800 I.U.	0	0	---	---	Neg.	Neg.
Menorrhagia	H. M. 30	Flowing 3 wk.	3 dilatation and curettage; "shots"	3,000 I.U.	Benefited	3-7 days' duration. Regular	Cullen's hyperplasia	Proliferation	---	---
	P. M. 27	Flowing 9 wk.	Rest; oral medication	4,200 I.U.	Benefited	Improvement for 4 mo. only	Secretory phase	Proliferation	---	---
	V. B. 23	Flow lasting 7 to 21 days	2 dilatation and curettage	3,000 I.U.	Benefited	Regular, 4-8 days' duration	Cullen's hyperplasia	Proliferation	---	---
	H. A. 24	Flowed 2 wk.	None	4,200 I.U.	Pregnant	Full term pregnancy	Proliferation	---	---	---

SUMMARY

Thirteen patients with amenorrhea and oligomenorrhea were treated with pregnant mares' serum. After eight months' observation, regular monthly periods have continued in 3 of the 13, 1 of the 3 having been a case of primary amenorrhea.

Four patients with menorrhagia were treated; all 4 of whom showed evidence of immediate improvement. One of the 4 became pregnant after a sterile marriage of five years, and has gone on to full term. Two of the remaining 3 have shown continued benefit after eight months.

Endometrial changes in the cases of amenorrhea and oligomenorrhea were inconstant, while in the cases of menorrhagia, the pattern changed from one of hyperplasia to one of proliferation.

The authors wish to express their indebtedness to Dr. Wm. H. Vogt, Sr., Director of the Department of Obstetrics and Gynecology, for his suggestions and invaluable aid in carrying out these studies.

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THE EFFECT OF ORAL ADMINISTRATION OF ALPHA ESTRADIOL AND PREGNENINOLONE UPON THE HUMAN CASTRATE UTERUS

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THE oral effect of estrin,[1] and the combined effect of oral estrin and parenteral progestin[2] upon the human castrate endometrium have been previously demonstrated. This presentation concerns itself with the application of oral estrin (dimenformon)* and an oral synthetic progestin derivative (pregneninolone)* upon the endometrium of the human castrate uterus. In addition, an attempt has been made to determine the standard for a human unit of these two ovarian hormones, i.e., the approximate amounts utilized, in milligrams, of crystalline substance during a normal menstrual cycle.

*We are indebted to Roche-Organon, Inc. for a supply of dimenformon and pregneninolone (progestoral).

CASE REPORTS AND EXPERIMENTAL PROCEDURES

CASE 1.—F. L.* white, female, married, aged 37 years, was subjected to bilateral salpingo-oophorectomy for cystic ovaries. Menstruation began at 14, was irregular with occasional intervals of from three to six months, always painful and profuse, at times lasting thirty days. There had been four full-term pregnancies. The castration syndrome developed six months postoperatively. A premedication endometrial biopsy was taken and a scanty amount of tissue obtained; diagnosis of this tissue was atrophic endometrium.

Bimanual Examination: Uterus anterior, freely movable; cervix well epithelized and measured 2½ inches from external os to fundus. Adnexa were not palpable. Vaginal mucosa was pale and dry.

Sept. 26, 1939, to Oct. 7, 1939: Dimenformon, 4 mg. daily, for twelve days.

October 8 to 19: Dimenformon, 6 mg., plus 75 mg. pregneninolone daily for twelve days.

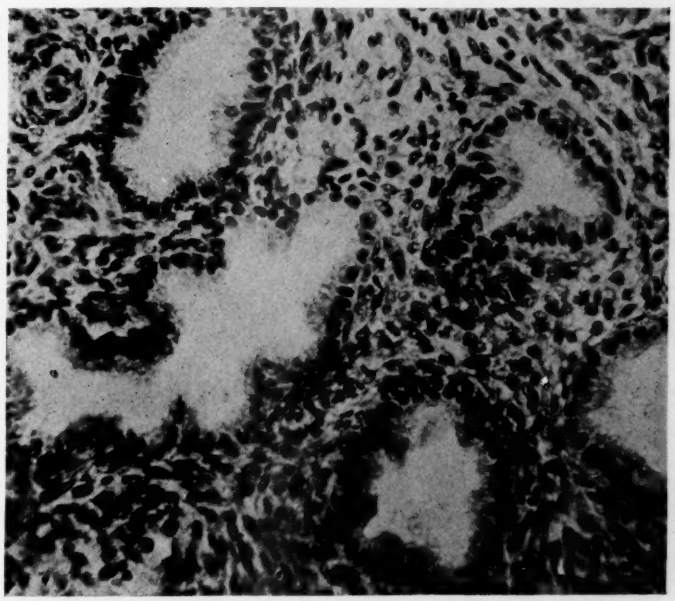

Fig. 1.—Early to midluteal phase produced with 120 mg. of estradiol and 900 mg. of pregneninolone. ×200.

October 21: Endometrial biopsy was taken and the diagnosis of an early to midluteal phase of endometrium established (Fig. 1).

October 23 to 26: Bleeding was reported.

The patient noted some increase in libido, flushes disappeared, and the uterine measurement from external os to fundus was 2½ inches; vaginal secretion was present and the vaginal mucosa was a normal, pinkish hue. For a period of three months she was comfortable, when menopausal symptoms reappeared.

CASE 2.—J. K.* white, female, married, aged 22 years, was admitted to the Gynecological-Endocrine Clinic, complaining of hot flushes and amenorrhea. Both ovaries had been removed at two previous operations, but the uterus was left in situ with a Crossen suspension. Menstruation began at 15 years of age, of three days' duration, and occurred every thirty days. For two years prior to operation she menstruated every two weeks for ten to eleven days, with a profuse flow and pain.

*These castrates, now receiving oral estrin and oral pregneninolone, were reported upon in a previous communication[2] after having been given oral estrin and parenteral progestin.

Last period four months previously. Flushes, accompanied by headaches, began soon after operation. Bimanual examination revealed a small uterus which was in anterior position, not freely movable. Adnexa were absent. Uterine measurement, from external os to fundus, was 2½ inches. A premedication biopsy was taken and a meager amount of endometrium obtained; the tissue was diagnosed as atrophic endometrium.

Dec. 25, 1939, to Jan. 5, 1940: Dimenformon 4 mg. daily for twelve days.

Jan. 6 to 17, 1940: Dimenformon 6 mg. plus 100 mg. pregneninolone daily for twelve days.

January 20: Biopsy taken. Diagnosis: mid- to late luteal phase of the endometrium (Fig. 2).

January 22 to 26: Bleeding was reported. Uterus measured three inches from external os to fundus.

The patient noted no change in libido but described breast stimulation. Flushes completely disappeared during medication.

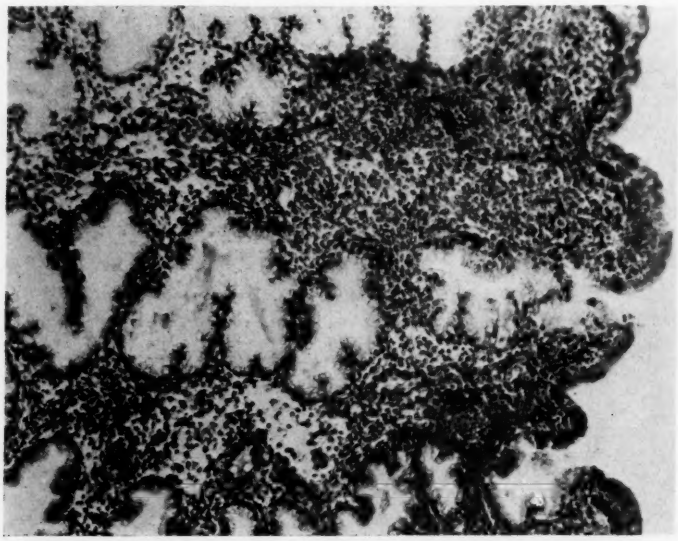

Fig. 2.—Late luteal phase produced with 120 mg. of estradiol and 1,200 mg. of pregneninolone. ×160.

CASE 3.—P. Z.,* aged 40 years, widow, was admitted to the Gynecological-Endocrine Clinic complaining of hot flushes every one-half to two hours, followed by attacks of excessive perspiration, joint pains over entire body, headache, and vertigo. Last menstrual period occurred eight months previously when a bilateral salpingo-oophorectomy for cystic ovaries was performed.

Bimanual examination revealed a small, atrophic, retrodisplaced uterus, measuring 2½ inches from external os to fundus. The vaginal mucosa was dry and pale. Cervix was atrophic and dilatable with extreme difficulty. Endometrial biopsy revealed atrophic remnants of an early follicular phase.

Dec. 24, 1939, to Jan. 4, 1940: Dimenformon, 4 mg. daily for twelve days.

Jan. 4, 1940, to Jan. 15, 1940: Dimenformon, 6 mg. plus 100 mg. pregneninolone daily for twelve days.

Jan. 18, 1940: A biopsy was taken and the diagnosis of the endometrial tissue was a late luteal phase (Fig. 3). At this time the uterus measured 2½ inches from external os to fundus.

January 18: There was spotty bleeding.

January 19 and 20: Patient reported bleeding which necessitated the use of five pads daily.

Flushes disappeared during medication and reappeared April 16, 1940.

*See footnote page 87.

CASE 4.—C. L.,* white, married, aged 28 years, was admitted to Gynecological-Endocrine Clinic complaining of hot flushes and nervousness, excessive perspiration, more marked during the night, and frequent frontal headaches. She had had a

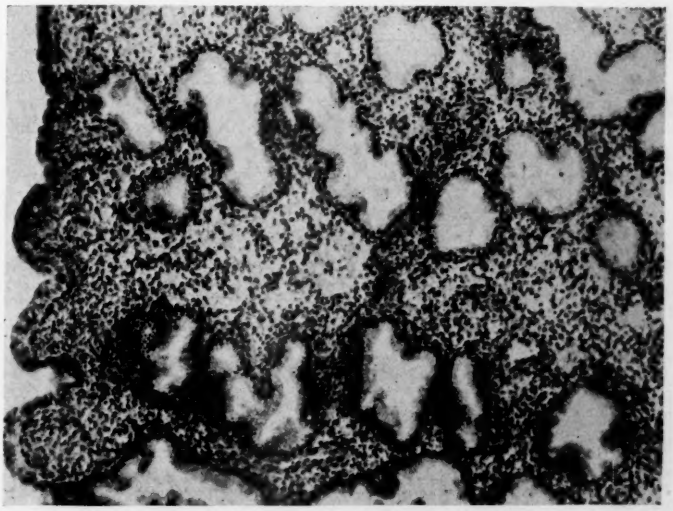

Fig. 3.—Mid to late luteal phase produced with 120 mg. of estradiol and 1,200 mg. of pregneninolone. ×160.

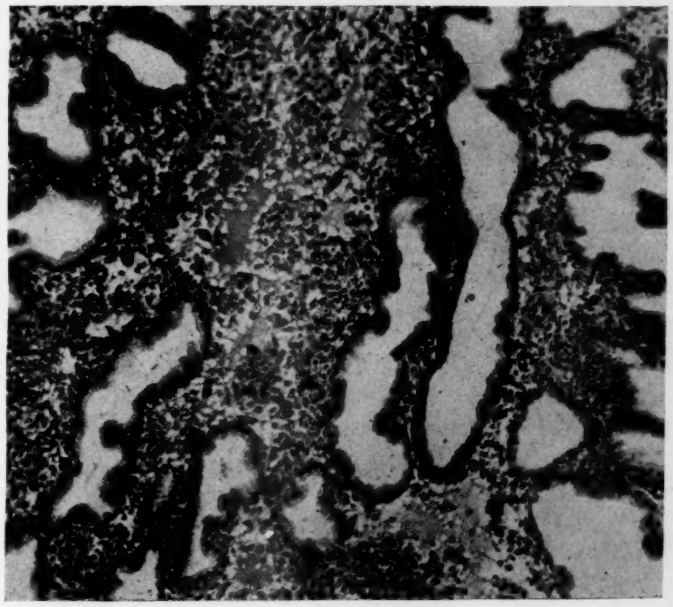

Fig. 4.—Mid to late luteal phase produced with 120 mg. of estradiol and 1,200 mg. of pregneninolone. ×160.

bilateral salpingo-oophorectomy four years previously for bilateral dermoid cysts. Menstruation began at 13 years of age and was of four days' duration, with irregular intervals. She had had two normal pregnancies and one spontaneous miscarriage. There had been no menstruation since operation.

*See footnote page 87.

Bimanual examination revealed the uterus to be slightly smaller than normal, in anterior position, freely movable, cervix small, well epithelizated; uterus measured 2¼ inches from external os to fundus. An endometrial biopsy specimen was diagnosed as atrophic endometrium.

Feb. 8 to 19, 1940 inclusive: Dimenformon 4 mg. daily for twelve days.

February 20 to March 2 inclusive: Dimenformon 6 mg. daily plus 100 mg. pregneninolone for twelve days.

March 5: An endometrial biopsy was taken and a moderate amount of tissue was recovered. Diagnosis was a mid- to late luteal phase of endometrium (Fig. 4). The uterus measured 2¼ inches from external os to fundus. Patient menstruated March 6 to 9, normal flow. Headaches, backaches and flushes disappeared during medication. Flushes began to reappear two months later.

CASE 5.—M. S., aged 33 years, married, had had no menses for seven years, but had hot flushes one to three times during the day, constant fatigue, headaches, and dizziness; bilateral salpingo-oophorcystectomy, appendectomy 1925, one miscarriage, one stillbirth; for about four or five years following operation, menses occurred every three to four months for two or three days, moderate flow.

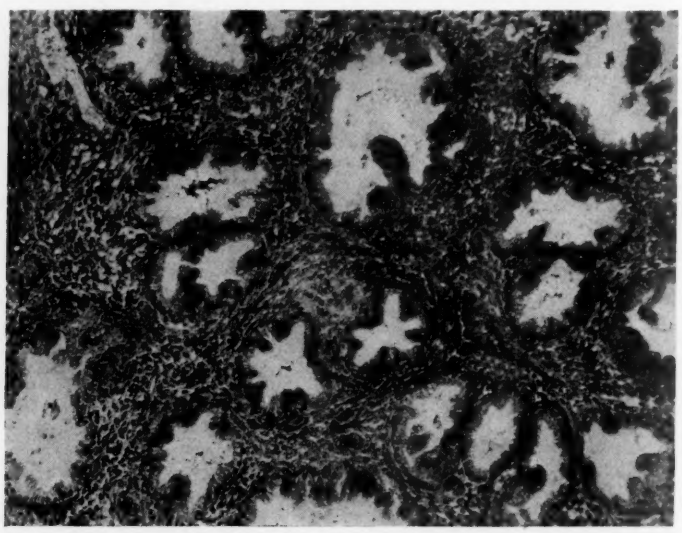

Fig. 5.—Late luteal phase produced with 120 mg. of estradiol and 1,200 mg. of pregneninolone. ×160.

Bimanual examination showed the external genitals to be atrophic, vaginal orifice small, and barely admitting two fingers; cervix atrophic, well epithelized; uterus retroflexed and measured 2 inches from external os to fundus, dilatation rather difficult.

March 28, 1940: An endometrial biopsy was taken and scant endometrium obtained. The diagnosis was atrophic endometrium.

March 30 to Apr. 10, 1940: Dimenformon, 4 mg. daily for twelve days.

April 9 to 20: Dimenformon 6 mg. daily plus pregneninolone 100 mg. daily for twelve days.

April 23: Patient reported beginning of staining. An endometrial biopsy was taken and a moderate amount of tissue was obtained which was diagnosed as mid- to late luteal phase (Fig. 5). At this time the uterus measured 2½ inches from external os to fundus. There was bleeding from April 23 to 30, necessitating the use of two pads daily.

The flushes disappeared during medication and there was no difficulty with cervical dilatation after treatment. The patient was seen Aug. 6, 1940, at which time she had no return of hot flushes.

COMMENT

The ultimate objective in the field of hormone therapy is replacement of the injectable endocrine products by oral medication. With this purpose in view, an attempt was made to produce, by means of oral medication in the human castrate, the actual changes occurring in the endometrium during a normal menstrual cycle. Many investigations have been made in the past with lower animals and primates, demonstrating the effectiveness of endocrine preparations. Yet it is well known that the differences between human and animal physiology prevent a common application of therapy. It is, therefore, desirable to utilize human physiology so far as possible, in order to ascertain definitely biologic potency.

Up to the present time the literature contains very few reports concerning pregneninolone, a new type of synthetic luteal hormone.

Inhoffen and Hohlweg[3] were able to produce a full-blown luteal phase in an infantile guinea pig uterus, previously stimulated with ethinyl estradiol, with 4 mg. of pregneninolone. Zondek and Rozin[4] report luteal endometrial changes in a previously estrinized secondary amenorrheics. In another instance bleeding similar to menstruation occurred several days after cessation of medication. Clauberg,[5] utilizing noncastrated amenorrheics, claims luteal changes following administration of 92 mg. of ethinyl estradiol plus 220 mg. of pregneninolone, 100 mg. of progynon C, and 300 mg. of pregneninolone, respectively. He never used more than 400 mg. of pregneninolone, and reports bleeding within six days of cessation of medication, yet none of his microphotographs really shows changes analogous to a normal twenty-two- to twenty-four-day endometrium. Salmon, Walter and Geist[6] have produced progestational changes in five postmenopausal women with 140, 480, 105, 500, and 540 mg. of pregneninolone, respectively, after intramuscular priming with amounts varying from 120,000 to 655,000 R. U. of estradiol benzoate. The second case showed a very good late luteal phase. There was no report of any bleeding after medication.

The dosage and timing of this investigation were based upon previously reported oral-parenteral experiments. In that series, 90 mg. of progestin parenterally over a twelve-day period produced endometrial changes comparable to a normal late luteal phase. In the present series, ten times that quantity was given orally to Case 1, 900 mg. in the form of pregneninolone, over a twelve-day period. An early to midluteal phase was produced; since this did not correspond to a late progestational phase, the dose in the other cases was stepped up to 13 times the amount. Cases 2, 3, 4, and 5 received therefore 1,200 mg. of pregneninolone over twelve-day periods and here the endometriums were of the late premenstrual type.

Bleeding which was described as menstruation occurred in all patients within forty-eight to seventy-two hours after cessation of medication. In addition, the usual premenstrual molimina were reported. Libido was increased in some and in others there was no change. Cases 2 and 5 showed some evidences of uterine growth. All degrees of atrophic changes disappeared with medication. Patients were completely free of the menopausal syndrome during medication and for some time afterwards.

As to a possible human unit, or the amounts of both hormones which are actually necessary to produce the desired endometrial changes, assuming that the ratio of effectiveness between oral and parenteral administration is 1:13; then in actual crystalline substance 9 mg. of estradiol and 90 mg. of progesterone are approximately the amounts utilized in normal menstrual cycles. Some investigators believe that the ratio varies from 1 to 6:8. This may be true if biologically active extracts were employed; however, the above findings are based entirely upon the use of synthetic preparations.

The value of this research problem offers future possibilities in the treatment of certain endocrine disturbances. In instances of atrophic uteri due to intrinsic changes, present-day methods of pituitary and ovarian stimulation, which are very questionable, are insufficient to reestablish normal menstrual cycles. The uterus must be in a state receptive to normal ovarian secretion. In many instances of secondary amenorrhea, usually preceded by months of hypomenorrhea, this does not exist, in spite of the presence of a normal pituitary-ovarian relationship. In this type of endocrine derangement, oral therapy of this kind should prove of value. At the present time oral therapy is beset with several difficulties, namely the necessity of high dosage and the consequent expense. With improved chemical methods, this expenditure may eventually be lowered, for small doses orally are of no value in severe endocrine dyerasias.

SUMMARY

Six female castrates were treated with synthetic oral estradiol and progestin. The total amount used was 120 mg. of estradiol and 900 to 1,200 mg. of pregneninolone. Progestational changes were produced in all cases. In four instances, the endometrium approximated that of a late luteal phase, whereas one with smaller dosage showed only an early luteal change. The symptoms and atrophic changes characteristic of the menopause completely disappeared during medication and returned months afterward in all patients with one exception. Uterine growth was manifest in two instances. Bleeding occurred in all patients within forty-eight to seventy-two hours after cessation of medication. The ratio of effectiveness between oral and parenteral administration is approximately 1:13.

I wish to express my grateful appreciation to Dr. Walter T. Dannreuther for his kind assistance and constructive criticisms, and to Miss Mary Chin for the preparation of the sections.

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ESTRIN POTENCY AND BASAL METABOLISM*

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EXPERIMENTS reported previously (Collett, Smith, and Wertenberger, 1937) have shown that estrin administration affects the basal metabolic rate appreciably. We have since tried to see whether the potency of the various estrins, given orally or by injection, could be assayed by their effect upon the basal metabolic rate.

Our subjects were five women, 30 to 42 years of age, who had been subjected to panhysterectomy. They were first studied three to nine months after operation. By means of daily metabolism tests, we established the reaction of each patient to varying doses of estrin given in the same form and by the same route, and then proceeded to a comparison of oral and injected doses of estrone or of oral doses of estrone and of estriol. The estrins used were: Estrone (oil theelin† and Ovex Leo tablets‡) and estriol theelol capsules.§

Except with Cases M and N, medication was continued daily for a week. Metabolism tests were made daily or on alternate days. Instead of indicating every metabolism test as heretofore, we show in the graphs only the average basal metabolic rate for each week; before, during, and after medication. The vertical lines in Charts 1 and 2 indicate the range of variation in each week. Basal metabolic rate is stated in percentage of the premedication level, which is always somewhat below the Harris-Benedict standard in these subjects.

The unequal effect of large and small doses given by the same route appears in all the graphs. The average basal metabolic rate of Patient K (Fig. 1) was raised 10 per cent by six daily doses of 500 I.U. oil theelin given by injection. A higher dosage (1000 I.U.) produced a smaller rise, 5 per cent. A similar difference in metabolic response to unequal dosage was observed in this patient on orally administered oil theelin: a rise of 9 per cent on 1000 I.U. and of 5 per cent on 2000 I.U. Patient L (Fig. 2) showed a rise in basal metabolic rate of 15 per cent on 500 I.U. injected oil theelin, but a smaller immediate rise (5 per cent) followed by a delayed rise of 10 per cent on 1000 I.U. doses. Patients M and N (Fig. 3) were given larger doses of injected oil theelin: one dose of 10,000 I.U. or 5 doses of 2,000 I.U. Patient M's basal metabolic rate fell 2 per cent in the week of the broken dose and 5 per cent in the week of the single large dose. Patient N's basal metabolic rate was unchanged in the week of medication, but in the second and third weeks showed a greater rise with the broken dose than with the single large dose. Patient O (Fig. 4), when given estrone (Ovex) orally, showed a drop in basal metabolic rate of 2 per cent on 1,000 I.U. and of 5 per cent on 2,000 I.U. Although the amount and direction of the change in basal metabolic rate varied with

*This experiment was done with the aid of a grant from the Council on Pharmacy and Therapeutics of the American Medical Association.

†Parke, Davis & Co.

‡R. A. B. Leo, Hälsingborg, Sweden.

§Parke, Davis & Co.

the individual, it is clear in every case that larger doses differed from smaller doses in causing a smaller rise or a greater fall in basal metabolic rate. We have, therefore, used this method for estimating the relative potency of estrone and estriol given orally, and of injected versus orally administered estrone.

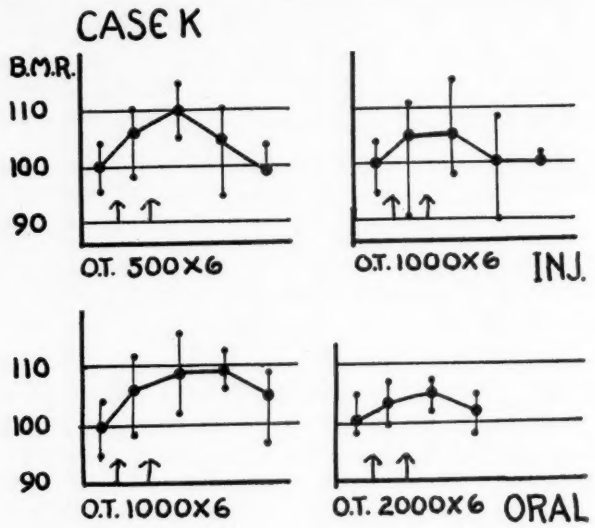

Fig. 1.

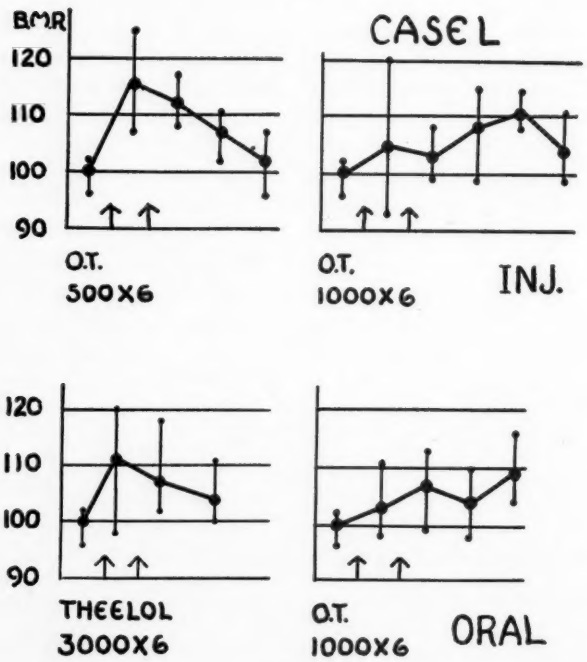

Fig. 2.

With Patient K. 1,000 I.U. injected estrone (oil theelin) produced a smaller rise than 1,000 I.U. taken orally, but a slightly greater rise than 2,000 I.U. taken orally. The potency of injected estrone was therefore almost double that of oral

estrone. With Patient L a comparison of basal metabolic rate averages indicates that 1,000 I.U. injected estrone (oil theelin) was slightly more potent than 2,000 I.U. of estrone (Ovex) taken orally. With Patient O, 1,000 I.U. injected estrone (oil theelin) gave a fall in basal metabolic rate of 5 per cent with a much delayed rise, while 2,000 I.U. estrone (Ovex) given orally caused an almost equal fall followed by a prompt rise of 10 per cent, indicating that estrone was a little more than twice as potent when injected than when given orally. Thus with all 3 patients, injected estrone seemed 1 to 2½ times as potent as the same dose taken orally.

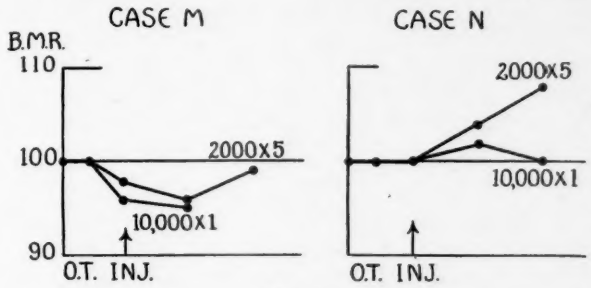

Fig. 3.

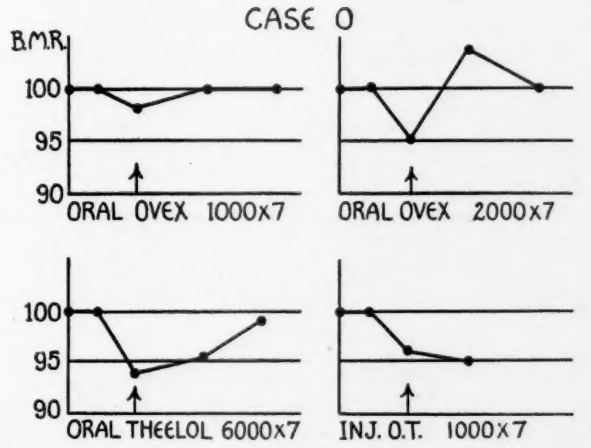

Fig. 4.

Orally administered estriol was compared with oral estrone in two patients. With Patient L, 3,000 I.U. (0.18 mg.) of estriol (theelol) led to an immediate rise of 10 per cent, slightly less than that induced by 500 I.U. injected estrone; while 1,000 I.U. oral estrone (oil theelin) led to a slower rise of 3 to 10 per cent. With this patient 1,000 I.U. oral estrone was, therefore, more potent than 3,000 I.U. oral estriol. With Patient O, 2,000 I.U. doses of oral estrone (Ovex) led to an immediate fall in basal metabolic rate of 5 per cent, followed in the next week by a rise of 10 per cent; while oral estriol (theelol) in 6,000 I.U. doses led to the same immediate drop and a slower rise. With Patient O, therefore, 6,000 I.U. of oral estriol seemed slightly more potent than 2,000 I.U. of oral estrone. In both patients, then, oral estriol appeared to be about one-half as effective as oral estrone, and about one-sixth as effective as injected estrone, unit for unit.

Daily reports on symptoms were made by all the patients, and these, in general, support the estimates of potency based upon basal metabolic rate fluctuations, although small differences are less definitely indicated. We have found that the patient's sense of energy is a clearer index of potency than the lessening of her hot

flushes. Patient K's reports indicated a slightly greater potency for injected than for oral estrone. Patient O's reports showed injected estrone about twice as potent as oral estrone and four to five times as potent as oral estriol. Patient L's reports (Fig. 5) showed injected estrone twice as potent as oral estrone and three to four times as potent as oral estriol. It was difficult to get accurate reports from the patients, and the difficulty was increased by the fact that medication was not continuous and was generally barely enough to diminish symptoms without abolishing them. When dosage is close to the optimal level for a given patient (as with Patients M and N), the subject is likely to report feeling better on consecutive small doses than on a large single dose, probably because a larger dose, unless continuous, upsets her endocrine balance.

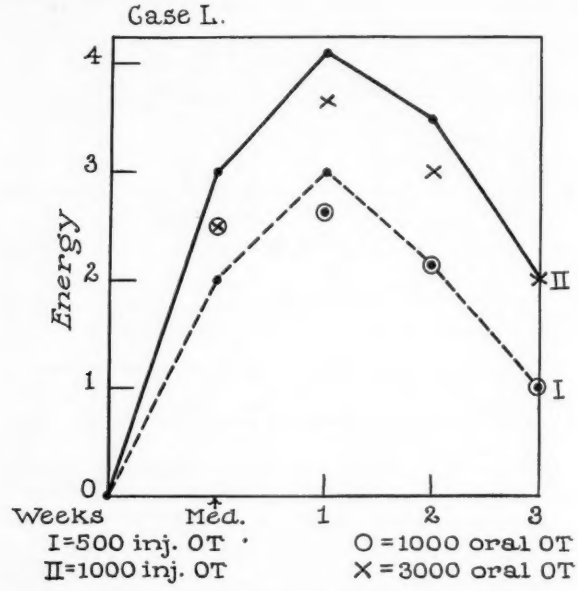

Fig. 5.

A more satisfactory estimate of potency based upon personal reports was obtained from a patient outside this series, who received continuous daily medication instead of medication for a single week. She was a woman of 30 whose ovaries were intact but functioning poorly. A record covering 3 consecutive menstrual cycles showed the results as shown in Table I.

TABLE I. CYCLE DAYS

CYCLE	DAYS		DAILY DOSAGE IN I.U. ORALLY	
	BAD	GOOD	OVEX	THEELOL
1	70	32	----	1000
2	57	43	----	1800
3	45	55	1800	----

Too low a dosage (1,000 I.U. theelol) gave a large proportion of days of extreme fatigue and nervousness. A larger dosage of theelol (1,800 F.V.) improved the record, and 1,800 I.U. of ovex (estrone) improved it still more. This result agrees with the estimate of the relative potency of these two estrins based upon basal metabolic rate fluctuation observed in our other patients.

It is worth noting that our records show all the effects of estrin upon basal metabolism reported by other authors: increase, decrease, and

no effect. It is now clear that this apparent chaos can be explained by the size of the dose in relation to the endocrine balance. It seems probable that the action of estrin upon basal metabolism is first through the thyroid directly and then indirectly by way of the anterior pituitary (Victor and Anderson).

A halving of potency by the oral route, such as we have observed with estrone, is found with many drugs, and agrees with the ratio observed by Mazer and Israel.

Our finding that oral estriol is less potent than oral or injected estrone disagrees with Rowe and Simond but agrees with Mazer and Israel, Nelson and Overholser, and D'Amour and D'Amour. D'Amour and D'Amour suggest that part of the difficulty may lie in the manufacturer's use of different methods of assay for the two substances.

SUMMARY

Relatively small doses of estrin produce a larger rise or a smaller fall in basal metabolism than do heavier doses given to the same individual. Differences in the potency of different estrins given by the same or different routes can, therefore, be estimated by means of the basal metabolic rate. On this basis, oral estriol appears to be less potent, unit for unit, than oral estrone; and oral estrone only slightly less potent than injected estrone.

We are greatly indebted to Professor Sollmann for advice on this work; to Dr. Joseph T. Smith and Dr. Robert Faulkner for referring patients from the Department of Gynecology at Lakeside Hospital; and to the Council on Pharmacy of the American Medical Association for a grant in aid.

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From a study of a large number of women with fibroids, ovarian cysts and carcinoma of the uterus, the authors conclude that uterine cancer occurs in short, heavy women, whereas fibroids of the uterus and ovarian cysts are found in thin individuals.

J. P. Greenhill.

THE INCIDENCE OF HYPERTENSION AFTER THE TOXEMIAS OF PREGNANCY

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THERE has been considerable difference of opinion regarding the subsequent effects of the hypertensive toxemias upon the maternal organism. The statement has been made that eclampsia never recurs, and that if the patient survives the acute disease, all of the signs and symptoms disappear promptly after delivery, that there are no subsequent ill effects, and that future pregnancies will not be complicated by a repetition of the toxemic signs and symptoms, or convulsions. On the other extreme, it has been occasionally intimated that the toxemic patient should never have subsequent pregnancies, because of the danger of a recurrence of the toxemia even possibly in a more serious form than with the previous pregnancy. It is likely that neither of these extremes is correct, for while some individuals may have a complete disappearance of all abnormal signs and symptoms after delivery and remain perfectly well without abnormal findings, and pass through subsequent pregnancies without any evidence of toxemia, there are others who show persisting hypertension after the toxemia and who have a recurrence of toxemic signs and symptoms even in a more severe form in following pregnancies. It is probable that the differences in these extremes are due to differences in etiology and in the underlying pathologic processes, but it is difficult to distinguish these differences unless the conditions existing before the pregnancy are known, as for example previously recognized essential hypertension or chronic nephritis, although either of these may first make their appearance during the course of a pregnancy.

In an effort to determine in our own clinic the frequency with which the hypertensive toxemias are followed by permanent hypertension, we have during the past several years attempted a follow-up study of these individuals. An effort was made to examine and study all living patients in whom a diagnosis of toxemia of pregnancy was made between January, 1925, and December, 1936, a period of twelve years. In all patients included in the study, at least one year had elapsed since the toxemia occurred and in over one-half of them five or more years had elapsed.

At the beginning of the study various tests for renal function and chemical determinations of the nonprotein nitrogenous constituents of the blood and eye ground examinations were carried out, but it was soon found that the most significant finding by which to determine the subsequent effects of the toxemia was the blood pressure determination. We have classified as hypertension, on the basis of repeated blood

pressure determinations, all patients in whom the systolic pressure was 140 mm. of mercury or more and the diastolic 90 or more.

TABLE I

	CASES	PATIENTS	DEATHS	DEATH RATE
Toxemia without convulsions	430	377	9	2%
Toxemia with convulsions	136	134	19	14%
Totals	566	511	28	4.9%

For the period under consideration there were 566 instances of hypertensive toxemia occurring in 511 patients. The toxemia had occurred more than once in the same patient in 55 instances, giving an incidence of recurrent toxemia of 10.7 per cent. Of the 511 patients, 28 died during their stay in the hospital, a mortality rate for the entire group of 4.9 per cent. Nine deaths (2 per cent) occurred in the nonconvulsive group, while 19 deaths (14 per cent) occurred in the convulsive group. Of the 483 patients who were discharged alive from the hospital, 7 were found to have died subsequently. Attempts at repeated follow-up examinations were successful in only 224 patients, a follow-up incidence of 47 per cent.

TABLE II

Patients discharged alive	483	
Died since discharge	7	
Patients not located	252	(53%)
Number with follow-up examinations	224	(47%)
Normal blood pressure at follow-up examinations	120	(53.5%)
Hypertension at follow-up examinations	104	(46.5%)

Of the 224 patients repeatedly re-examined, 104, or 46.5 per cent, had definite hypertension from one to thirteen years after the toxemia. If it may be presumed that this ratio is preserved in those who could not be re-examined, then it may be concluded that a patient with toxemia has almost a 50 per cent chance of a subsequent persistent hypertension. Blood pressure determinations of a comparable group after normal pregnancies and with similar age distribution revealed an incidence of hypertension of 12 per cent, which is approximately the average incidence of hypertension in the female during the reproductive period. So, it seems safe to assume that the toxemic pregnancy must have played a significant part in the high incidence of hypertension found in the follow-up examinations.

In an attempt to determine what factors might be present to influence the persistence of hypertension, the cases were tabulated and analyzed according to age, parity, convulsions, blood pressure levels at the time of the toxemia, and the severity of the toxemia.

TABLE III. AGE AT TIME OF TOXEMIA AS FACTOR IN RESIDUAL HYPERTENSION

AGE	TOTAL EXAMINED	HYPERTENSION	PER CENT
19 and below	62	12	19.4
20 to 24	53	18	34
25 to 29	27	15	55.5
30 to 34	37	23	62.2
35 to 39	29	23	80
40 and over	16	13	81.3

In Table III the patients are grouped into five-year age periods, and the findings clearly reveal an increased incidence of residual hypertension as the age advances. Those patients who were less than twenty years of age at the time of their toxemia only had a 19 per cent incidence of hypertension while those who were thirty-five years or more had an 80 per cent incidence.

TABLE IV. PARITY AS FACTOR IN RESIDUAL HYPERTENSION

	TOTAL	HYPERTENSION	PER CENT
Primipara at time of toxemia	113	30	26.5
Multipara at time of toxemia	111	74	66.5

When the cases are divided into parities regardless of age, it is found that the incidence of residual hypertension after toxemia with the first pregnancy is 26 per cent, while after multiparous pregnancies, the incidence is 66 per cent. It is obvious, of course, that the primiparous individual is usually in the younger age groups, so that the factors of age and parity operate inseparably. All the multiparous individuals are grouped together, as there seemed to be no appreciable differences for the various parities, and when subdivided, the individual groups were too small to be significant.

TABLE V. TYPE OF TOXEMIA

	NO.	HYPERTENSION	PER CENT
Mild pre-eclamptic	48	26	54
Severe pre-eclamptic	117	55	47
Chronic nephritis	4	4	100
Essential hypertension	5	5	100
Total nonconvulsive	174	90	51.7
Mild eclampsia	34	9	26
Severe eclampsia	16	5	31
Total convulsive	50	14	28

In Table V the re-examined patients are grouped on the basis of the type of toxemia which occurred. Except for the 9 instances of previously recognized nephritis and essential hypertension, the type of toxemia seems of no particular significance in regard to subsequent hypertension. There is no appreciable difference in the incidence following mild or severe pre-eclamptic toxemia, nor is there any significant difference in the incidence between mild and severe eclampsia. Hypertension occurs subsequent to a nonconvulsive toxemia almost twice as frequently as after a convulsive toxemia. Eclampsia, however, occurs most frequently in the younger age groups, and in primiparas, and has, of course, a higher death rate, so undoubtedly the factors of age, parity, and the higher death rate at the time of the acute illness account in some degree for the higher incidence of residual hypertension after a nonconvulsive toxemia. In general, the severity of the toxemia plays no appreciable part in the frequency of later hypertension, and is of no particular significance in attempting to prognosticate the occurrence of later hypertensive phenomena.

The relationship between the systolic blood pressure at the time of admission to the Hospital for the toxemia and the later hypertension is shown in Table VI. In general, the higher the systolic pressure at the time of the toxemia the greater are the chances of residual hypertension. Whereas with systolic pressures less than 180, about one-third are followed by hypertension, about one-half are followed by hypertension when the systolic pressure is between 180 and 220, and about three-fourths when the original pressure was between 220 and

TABLE VI. SYSTOLIC BLOOD PRESSURE AT TIME OF TOXEMIA ADMISSION

SYSTOLIC	NO. PATIENTS	NO. SUBSEQUENT HYPERTENSION	PER CENT
240	9	9	100
220	7	5	71
200	18	9	50
180	49	25	51
160	93	28	30
140	48	16	33

240, while it occurred in all of those in whom the original reading was 240 or more. While the results are not entirely conclusive, in general it may be surmised that the higher the systolic blood pressure at the time of the toxemia, particularly above 200 mm., the greater the possibility of persistent high blood pressure.

TABLE VII. DIASTOLIC BLOOD PRESSURE ADMISSION

DIASTOLIC	NO. PATIENTS	NO. HYPERTENSION	PER CENT
180	1	1	100
160	9	7	77
140	17	10	58
120	71	31	44
100	117	47	40
90	9	5	55

The cases are analyzed in Table VII on the basis of the diastolic blood pressure at the time of admission for the toxemia, and the figures do not reveal any very conclusive relationship, unless the diastolic pressure was at a very high level. When the diastolic pressure was above 160 mm., at least three-fourths of the patients had subsequent hypertension, while the incidence was about the same for the various levels below 160. However, the number of cases in the higher levels are so few that the results are probably not significant.

TABLE VIII. EFFECT OF SUBSEQUENT PREGNANCIES

PREG. SINCE	NO. PATIENTS	HYPERTENSION	PER CENT	NO. REPEAT TOXEMIA
Nonconvulsive				
0	34	6	17	--
1	19	5	26	9
2	10	3	30	7
3	5 (42)	2 (15)	40 (35%)	2 (23-54%)
4	5	3	60	3
5	3	2	66	2
Convulsive				
0	18	3	16	--
1 to 4	19	6	32	--

Of the 224 patients re-examined, 113 of them were primiparas at the time of their toxemia, 37 of whom had eclampsia. In Table VIII, we attempt to analyze these cases in relation to the effects of subsequent pregnancies. The table shows, without consideration of the age factor, that in individuals with toxemia during their first pregnancy, but who at the time of the follow-up examination had had no other pregnancies, the incidence of hypertension was 16 per cent after eclampsia, and 17 per cent after toxemia without convulsions. On the other hand when subsequent pregnancies occurred, the incidence of hypertension was prac-

tically twice as high, 32 per cent in the convulsive group and 35 per cent in the nonconvulsive group. The incidence of permanent hypertension increases almost proportionately to the number of subsequent pregnancies. Of the 42 women who had other pregnancies, 23 or 54 per cent had toxemia with their later pregnancies. It seems then from these findings that an individual, who as a primipara has a toxemia of pregnancy, has a 50 per cent chance of a toxemia with a subsequent pregnancy and at the same time is enhancing the possibility of a permanent hypertension with each succeeding pregnancy.

In our follow-up studies, an effort was made to find some correlation between the average normal weight of the individual, the weight gain during the pregnancy, and the incidence of subsequent hypertension, but no constant relationship could be determined. Likewise, an attempt was made to ascertain any causal relationship between urinary tract infections and the appearance of hypertensive toxemias, but no constant association could be found on the basis of our examinations and review. At times infections of the upper urinary tract were found in association with toxemia, but even more frequently urinary tract infections occurred without any evidence of hypertensive toxemia, while the toxemias commonly occurred without any of the common clinical or laboratory evidence of infection in the urinary tract. There was nothing in our studies to suggest that pyelitis or pyelonephritis played any constant or significant part in either the causation of the toxemia or the frequency of the residual hypertension.

SUMMARY

The hypertensive toxemias of pregnancy seem to be characterized essentially by a generalized arteriolar spasm. If the spasm is neither too severe nor too prolonged, the patient may have a complete recovery afterward without any evidence of permanent damage, and pass through additional pregnancies uneventfully. On the other hand, recovery may seem complete, but the toxemia recurs in a subsequent pregnancy, while in others various degrees of hypertension persist, and occasionally a malignant type of vascular renal disease may ensue with a fatal outcome in a fairly short space of time. In our attempts to carry out follow-up studies on 483 patients who had had toxemia of pregnancy from one to thirteen years previously, 7 were known to have died, presumably of vascular renal disease. Of the 224 patients who were re-examined 104, or 46 per cent, had hypertension on the basis of the commonly accepted criteria for hypertension. Of the 42 women who had had pregnancies subsequent to their first pregnancy with toxemia, 54 per cent had toxemia with their later pregnancies, while on the other hand 46 per cent had repeated their pregnancies without a recurrence of the toxemia, and 53 per cent had a normal blood pressure at the time of the follow-up examination.

The age and parity of the patient at the time of the toxemia seem to be the most significant factors in the incidence of subsequent hypertension: the younger the patient the less the chances of permanent hypertension, whereas the older the patient the greater the chances, approximately 80 per cent of those above thirty-five years of age having hypertension. The primiparous patients have an incidence of hypertension of

26 per cent, while toxemia in the multiparous patient is followed by an incidence of 66 per cent. Pregnancies subsequent to the toxemic pregnancy seem to be definite factors, for when pregnancy is repeated in the patient who has had toxemia, the chances of later hypertension are twice as great as in those who do not repeat their pregnancies, and the risk is increased with each subsequent pregnancy.

The severity and the type of the toxemia, except instances of previously known chronic nephritis or essential hypertension, seem of no special significance in the frequency of hypertension. There is a lower incidence following eclampsia, but the tendency of eclampsia to occur in the young primipara and the higher primary mortality rate in the severe forms of eclampsia are probably the factors which are operating to explain in some degree the difference in incidence of hypertension following the convulsive and nonconvulsive types. The height of the systolic and diastolic pressures at the time of the toxemia, except at the very high levels, seem to play only a small part in the incidence of later hypertension.

Except in cases of previously known nephritis and hypertension, there are no definite criteria by which the possibility of permanent hypertension following the toxemia can be predicted with certainty, although, in general, the chances are much less in the young primipara, whereas the chances in the older multiparous individuals, particularly those who repeat their pregnancies, are much greater. The individual who has had toxemia should be observed afterward, and if hypertension persists, additional pregnancies should be undertaken with considerable reluctance and with a very careful prenatal regime. On the other hand, about half of the patients will have no persisting hypertension and may go through subsequent pregnancies without ill effects or permanent damage.

PROTEIN AND HEMOGLOBIN IN NORMAL AND TOXIC PREGNANCIES

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IT IS now believed that the edema so commonly seen in toxic pregnancies is due in part to hypoproteinemia which results from dietary protein deficiency.[1, 2] Experiments on dogs[3] have shown that the protein intake is not only related to the production of serum protein but also related to the production of hemoglobin. In this work, protein and hemoglobin were removed from the circulation of some of the animals, while in others the hemoglobin in the form of washed red cells was reinjected and their only loss was in the plasma. Thus, in certain respects, the rapidly increasing removal of all the products necessary for its growth by the fetus from the maternal circulation was simulated.

This study was undertaken, therefore, with the purpose of investigating the relationship of the diet to anemia and hypoproteinemia and of their relationship to the occurrence of the toxemias of pregnancy.

Since the prenatal clinic of the Philadelphia General Hospital accepts only those on relief or in quite similar financial circumstances, it was assumed that little animal protein food could be purchased, since this is one of the most expensive items in an ordinary diet. Dietary protein deficiencies were expected.

METHOD

Serum protein and chemical hemoglobin determinations were made on each new prenatal clinic patient. If the hemoglobin was low, a red cell count was done. Out of the new cases for each day, 3 were chosen to be followed with repeated determinations, namely, the one with the lowest protein, the one with the lowest hemoglobin, and the one with a normal value in both. A dietary survey was made for as many of these cases as possible. A qualified dietitian gave each woman a form to be filled out with the quantities of all foods eaten for a week. Many of the patients were irresponsible and illiterate, so that only a few could be successfully followed and only a few (71 cases) returned the diet sheets in any form that was good enough for analysis by the dietitian.

Patients were admitted for toxemia when the systolic pressure reached 100, or when other symptoms appeared in sufficient degree to warrant admission. Serum protein, a/g ratio and hemoglobin determinations were made on admission. No attempt was made to suggest therapy, either in the clinic or on the ward.

FINDINGS

About 20 per cent of the prenatal clinic patients showed a protein of 6.0 Gm. or less on their first visit. The protein findings are usually arranged so that the values for patients in the same month of pregnancy appear together.

TABLE I. THE OCCURRENCE OF HYPOPROTEINEMIA IN CLINIC PATIENTS BY MONTHS

Month of pregnancy	2	3	4	5	6	7	8	9
Total number of patients studied for protein	22	43	73	91	69	64	43	51
Per cent with low protein	18.1	9.3	16.5	15.5	23.1	17.1	23.2	25.4

There were a number of women who remained well while their protein levels were low, but there were also a number who had more or less marked symptoms of toxemia. In the line which shows the percentage of the low group (6 Gm. or less) who were toxic, the number was highest in the group found low in the fifth month but remained high for all the succeeding months.

TABLE II. THE OCCURRENCE OF TOXEMIAS AMONG THE LOW PROTEIN GROUP

Month of pregnancy	2	3	4	5	6	7	8	9
Percentage of the low group who were toxic	0	25	50	69.2	50	36.6	33.3	26.0

When the patients were divided into a group who became toxic and a normal group, it was found that the number with hypoproteinemia was greater in the former than in the latter. After the protein levels of the two groups had remained the same, viz., between 6.6 and 7.5 Gm. for the first seven months of pregnancy, the level of the toxic group fell below that of the normal group, which remained at the previous level to the end.

The results of determinations repeated three or more times on each patient appear in Tables IV, V, and VI. In the first two of these tables, low protein means that one or more values of 5.6 Gm. or less was obtained in the time stated. In the third, low protein means that the average of all determinations during pregnancy were low.

TABLE III. HYPOPROTEINEMIA FOUND ON FIRST CLINIC VISIT OF PATIENTS WHO BECAME TOXIC

Month of pregnancy	2	3	4	5	6	7	8	9
Number of normal patients studied for protein	20	21	48	60	47	51	36	43
Percentage of normal patients with low protein	20	14.2	12.5	3.3	19.1	13.7	19.4	18.6
Average protein for normal patients	6.9	7.1	6.8	6.9	6.6	6.7	6.7	6.8
Number of toxic patients studied for protein		13	25	31	22	14	7	8
Percentage of toxic patients with low protein		8.3	28.3	29.0	26.3	21.0	42.8	62.5
Average protein for toxic patients (first clinic visit)		7.4	6.4	6.6	6.7	6.5	6.1	5.8

Women with low protein in both the second and third trimesters of pregnancy were much more common among the toxic cases than among the normal ones, while women with low protein in either trimester alone were as likely to belong to one group as the other.

TABLE IV. PROLONGED HYPOPROTEINEMIA AND TOXEMIA

	NORMALS (27)	TOXICS (19)
Number with low protein in both second and third trimesters	1	8
Low in second trimester only	3	3
Low in third trimester only	12	7
Normal protein throughout	11	1

Those whose protein had remained normal throughout pregnancy did not become toxic, with one very mild case excepted, but some whose protein was low remained normal. If the protein is below 5.6 mg. on only one occasion, the patient is not nearly so likely to be toxic later as is the woman whose protein values have averaged 6.0 Gm. or less.

TABLE V. SIGNIFICANCE OF OCCASIONAL HYPOPROTEINEMIA

	NORMALS (27)	TOXICS (19)
Normal protein throughout	11	1
Low protein on any occasion	16	18
	X^2 is 7.27	P is less than 0.01

TABLE VI. SIGNIFICANCE OF LOW PROTEIN AVERAGE

	NORMALS (27)	TOXICS (19)
Normal protein average	18	4
Low protein average	9	15
	X^2 is 9.23	P is less than 0.0

Among the patients who were hospitalized for toxemia, there were some who were less toxic than others. The figures from all patients hospitalized appear in Table VII.

Nearly all of the patients hospitalized had low protein. The a/g ratio was not under one (or inverted) except in two cases (9 per cent), but it was often decreased toward one. According to the fall of the a/g ratio value in proportion to the decrease in total protein, the patients could be divided into three groups. In the largest group, the fall of total protein was great but the ratio remained nearly normal. In the second group, almost equally large, the fall in both values was

TABLE VII. DATA ON PATIENTS HOSPITALIZED FOR TOXEMIA

INITIALS	PROTEIN	ALBUMIN	GLOBULIN	A/G RATIO	HEMOGLOBIN	INTERVAL BEFORE OR AFTER	BLOOD PRESSURE AND OTHER DATA
1 J. M.	5.2* Gm.	2.1	3.1	0.7			200/124, eclampsia, hepatomegaly, positive Takata-Ara test
	7.4	2.5	4.5	0.5	9.0	23 days after	
2 D. T.	7.8				11.6	90 days before	Eclampsia
	5.9*	3.7	2.2	1.7			Dead child
3 B. S.	6.3				13.4	90 days before	Post-partum convulsions
	4.4*						Excessive weight gain
4 W. S.	7.7				10.4	70 days before	Pre-eclampsia, 157/60
	6.0*	3.4	2.6	1.3			Excessive weight gain
	6.4	4.0	2.4	1.7		70 days after	
5 C. McD.	6.5				10.0	60 days before	Severe pre-eclampsia, 175/110
	6.0*	3.7	2.3	1.6			
6 C. S.	9.7				12.0	90 days before	180/100
	6.3	3.5	2.8	1.3		10 days before	
	5.2*	3.5	1.7	2.0			
	5.8	3.3	2.5	1.3		10 days after	
7 B. S.	5.9				14.0	100 days before	155/110, albumin 4-plus
	4.1*	2.8	1.3	2.1			Edema 2 plus. She had convulsions after previous pregnancy
	4.5	3.0	1.5	2.0		4 days after	
	4.8	3.1	1.7	1.8		11 days after	
	6.9	4.7	2.2	2.1		18 days after	
8 R. W.	8.5				15.2	105 days before	170/130, albumin 4-plus, excessive weight gain, edema 1-plus. Blood uric acid 5.0 mg.
	4.6*	3.1	1.5	2.0			
	5.0	2.6	2.4	1.1		5 days after	
	6.9	4.0	2.9	1.4		12 days after	

9 J. B.	6.4 6.7*	4.0	2.7	1.5	11.5	180 days before	150/100, albumin 4-plus, edema 3-plus
10 M. P.	6.8 5.2 3.4*	3.9 2.3	1.3 1.1	3.0 2.0	11.3	105 days before 42 days before	Delivery of dead child
11 A. B.	6.9 5.3*	4.2	1.7	2.1	13.0	45 days before	190/130, delivery by cesarean, severe toxemia
12 R. Z.	6.7 5.9*	4.2	1.7	2.1	11.1	60 days before	Mild toxemia
13 J. S.	6.7 5.8	4.1	2.6	1.6	12.2	3 days before	Died of eclampsia 4 days later
14 A. D.	7.5 4.9*	4.0	0.9	4.0		180 days before	Eclampsia, 164/110 Albumin 4-plus. Edema 2-plus
15 E. D.	5.9	3.2	2.7	1.2	10.2		Eclampsia? 162/110
16 R. K.	6.0	3.6	2.4	1.5			Pre-eclampsia 205/110
17 M. J.	5.2	3.4	1.8	1.9			Convulsion 170/100
18 M. W.	4.9	3.5	1.4	2.5			168/80, eclampsia
19 D. H.	5.3	3.7	1.3	2.3			Severe eclampsia
20 D. J.	6.0	5.0	1.0	5.0			155/110
21 L. H.	5.0	1.9	3.7	0.6			Hyperemesis earlier
22 H. D.	5.9	4.2	1.7	2.5			Mild toxemia
Average values*	5.4	3.4	1.9	1.8	11.8	Number with inverse ratio 2	Per cent with inverse ratio 9

*Signifies that the value given was obtained at the height of symptoms, or nearly so.

proportionate. In a third group, the fall in the ratio value was great although the total protein value was normal or nearly so. The ninth case in the table shows this tendency, while the eleventh belongs to Group 1 and the second to Group 2. In some cases, as for example, the sixth, more than one group is represented among the figures. On the day when the symptoms were at their height, 12 of the patients had high ratios and 8 had low ones.

The previous protein values may have been over 6.0 Gm. until a few days before admission, but a fair number showed a fall in level during the eighth or ninth month, only one case having had low values on all previous examinations.

After delivery, the values rose toward normal. The finding of an average of only 5.4 Gm. for 22 cases at the height of their symptoms may be considered significant. The averages appear at the bottom of Table VII.

One case of hyperemesis gravidarum in early pregnancy followed by late toxemia appears in the table. There were two other cases which could not be put in the table because the patients did not have later toxemia. The first of these had 5.0 Gm. of protein five days before admission. On admission, it was 5.2 Gm. with an a/g ratio of 1.9. Sixteen days later it was 5.0 Gm., at which level it remained until forty-eight days from admission, but the patient did not develop toxemia of late pregnancy. The third woman with hyperemesis had 4.9 Gm. on admission and died of the disease in five days.

Table VIII shows the figures for the hemoglobin determination. There were more women whose hemoglobin was below 10 Gm. toward the end of pregnancy than in the earlier months. The normal and the toxic cases both averaged 11.5 Gm.

In Table IX, the patients with low hemoglobin were grouped according to the color index and cell count. Most of them were hypochromic anemias.

TABLE VIII. OCCURRENCE OF ANEMIA IN THE CLINIC

Months of pregnancy	2	3	4	5	6	7	8	9
Number studied for hemoglobin	21	35	76	92	75	67	43	48
Per cent with 10 Gm. or less	5	5.7	5.2	21.8	20	13.4	7	27.2

TABLE IX. TYPE OF ANEMIA

		AVERAGE HB.	AVERAGE CELL COUNT
All cases studied for type of anemia	23	9.2	3,240,000
Hyperchromic type	5	10.1	2,920,000
Hypochromic type	18	8.9	3,977,000

If 1.5 Gm. of protein per kilo of body weight be taken as the standard for women in the second and third trimesters of pregnancy, only 5 out of the 71 patients whose diets were analyzed ate the standard amount. Their average intake per day was 1.1 Gm./kilo, for both toxic and normal pregnancies. Out of 16 patients who ate only 0.9 Gm. or less, only one had a serum level of more than 6.5 Gm., and this individual later became toxic and the serum level fell.

The individual cases do not show a close correlation between protein intake and serum level. Two possible factors are at work here. Vomiting was severe in several of the women whose serum level was low in spite of a good intake. Utilization of the ingested protein for making serum protein is apparently more complete in women whose intake is low than in those who had a normal diet. This explains why some of the women on low diets did not show very low serum levels. In Whipple's dogs, the number of grams of serum protein manufactured per gram ingested rose as the diet was made progressively poorer. There may be other factors, but in spite of these, a rough relation between the intake and the serum level could be noted.

The intake for the women who later became toxic averaged the same as that of the normals, but the normal women were able to maintain a serum level one-half a gram higher on the same intake.

In the same group of 16 women who ate less than 0.9 Gm. each day, none had hemoglobin levels over 11 Gm., and most were below 10. The correlation between iron intake and hemoglobin level was poor. The average iron intake was 10 mg. per day for the group.

CONCLUSIONS

1. A large number of women were studied for anemia and hypoproteinemia in the Philadelphia General Hospital, and the findings are presented.

2. Hypoproteinemia seems to be a reasonably constant finding in both hyperemesis gravidarum and toxemia of late pregnancy. Not many women had toxemia of late pregnancy without some previously existing hypoproteinemia. It has been shown, however, that very prolonged hypoproteinemia was not necessary to the development of toxemia and that some patients on diets sufficient for others to maintain good serum levels go into hypoproteinemia and toxemia. In any attempt to give the etiology of these cases, some factor other than chronic dietary deficiency, some factor which is capable of lowering the serum protein level within a few short days must be sought.

3. The finding of a low serum protein value in a woman in the last trimester of pregnancy is often a warning of impending toxemia, especially if the protein has been normal earlier.

4. The severe anemias were not uncommon in the clinic, but they caused no trouble to any of the patients. Most of them were of the hypochromic type. The relationship between low protein intake and poor hemoglobin formation, earlier reported in dogs, was confirmed in pregnant women. No correlation between serum protein and hemoglobin level nor between the latter and the occurrence of the toxemias was apparent.

I wish to thank Dr. Philip F. Williams and Mrs. Florence G. Fralin for permission to use the data on the diets of these women and for their help and encouragement; also the members of the Department of Chemistry (Postgraduate Hospital) for their advice to me in the chemical determinations.

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THE EFFECTS OF TESTOSTERONE PROPIONATE, METHYL TESTOSTERONE, ANHYDRO-OXY-PROGESTERONE AND PROGESTERONE UPON LACTATION IN THE NURSING HUMAN BEING

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IN A previous report, it was pointed out that, though afterpains or painful engorgement of the breasts can be adequately relieved by small doses of testosterone propionate (10 to 15 mg.), lactation was not interfered with, provided the baby continued to nurse.[1] Others,[2-4] however, using 40 to 150 mg. of this steroid, have claimed successful inhibition of lactation in the human being. In order to verify our previous observations, the following studies were carried out, using larger dosages of testosterone propionate than any previously reported. In addition, methyl testosterone, anhydro-oxy-progesterone (pregneninolone, ethinyl testosterone), and progesterone were also studied as to their effects upon the initiation of lactation and the maintenance of established milk secretion.

PROCEDURES AND RESULTS

The mothers and babies used in these studies were carefully selected according to the criteria set up in a previous study.[5] Each gave a history of having adequately nursed a previous child for at least three months. Every one had had a normal spontaneous delivery of a seemingly normal active infant. Starting on the third day, the baby went to breast for twenty minutes at four-hour intervals five times a day. At 2 A.M., a dilute formula was substituted for the breast feeding. By weighing each baby before and after each breast feeding, the daily amount of mother's milk obtained was computed by totaling the results of the five feedings. A minimum of seven and one-half ounces daily was accepted as normal after the third post-partum day.

Fifty mothers served as controls, while there were 36 in the test groups.

Testosterone Propionate.—There were 12 patients in this group. To observe the effect of testosterone propionate upon the onset of lactation in the nursing human being, 6 of these received from 200 to 300 mg. of testosterone propionate in sesame oil intramuscularly over a period of two to five days, beginning soon after parturition. In not one instance was the onset of normal adequate lactation delayed (Fig. 1).

To note the effect of testosterone propionate upon established lactation, the other 6 patients received from 250 to 500 mg. of testosterone propionate intramuscularly over a period of two to four days, twenty-four to seventy-two hours after adequate milk secretion had been established. No effect whatsoever was noted upon the amount of milk secretion or upon the baby's gain in weight (Fig. 2).

The effect of testosterone propionate upon painfully engorged breasts has been reported elsewhere.[1]

Clearly, then, provided the baby continues to nurse, testosterone propionate will neither inhibit the normal onset of adequate lactation nor suppress the normal amount of milk secretion after adequate lactation has once been established.

Methyl Testosterone.—For the purpose of investigating the effects of this steroid, 10 patients were divided into 2 groups of 5 each. Beginning soon after parturition,

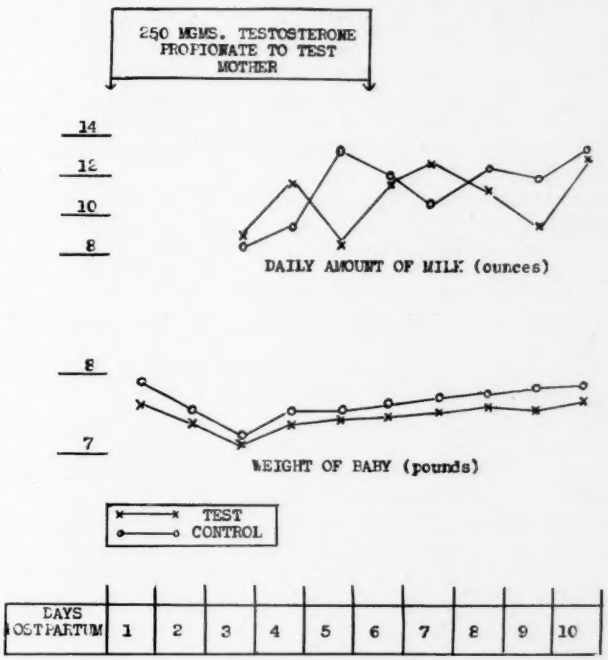

Fig. 1.—Failure of 250 mg. of testosterone propionate to inhibit the onset of adequate lactation in the nursing human being. Similar findings were obtained with either 500 mg. of methyl testosterone or 100 mg. of progesterone, as well as with 500 mg. of pregneninolone.

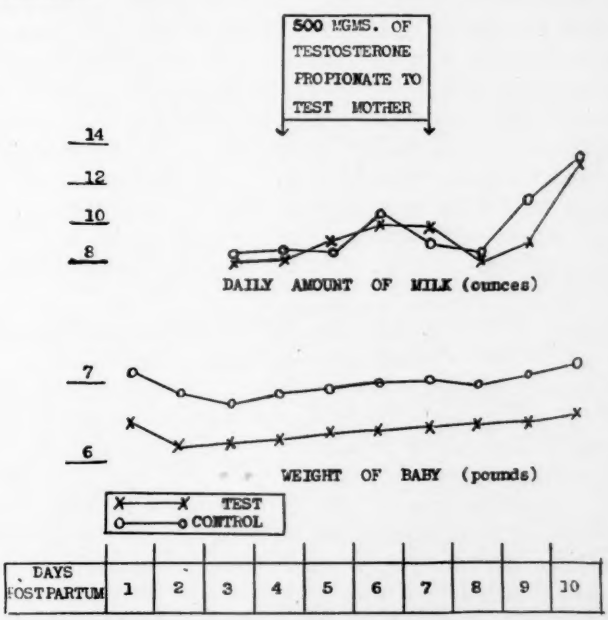

Fig. 2.—Failure of 500 mg. of testosterone propionate to suppress established lactation in the nursing human being. The result illustrated here is similar to that obtained with either 500 mg. of methyl testosterone or 100 mg. of progesterone, as well as with 500 mg. of pregneninolone. Essentially similar results were noted with 500 mg. of oral stilbestrol.[5] Normal variation ranges from one to seven ounces daily.

the first group received from 100 to 500 mg. of methyl testosterone in divided oral doses over a period of one to four days. The babies continued to nurse as usual. The onset of adequate lactation was not inhibited (Fig. 1).

In order to observe the effect upon established lactation, the other 5 mothers received from 250 to 500 mg. in divided oral doses twenty-four to seventy-two hours after milk secretion had become adequately established. Lactation was not suppressed (Fig. 2).

Anhydro-Oxy-Progesterone (Pregneninolone, Ethinyl Testosterone).—The effect of this steroid upon the initiation of milk secretion was studied in 5 patients. From 100 to 500 mg. were administered orally in divided doses over a period of one to four days, beginning soon after delivery. The onset of lactation was not affected (Fig. 1).

The effect upon established milk secretion was then studied. From 250 to 500 mg. were administered orally over a period of one to four days, starting twenty-four to seventy-two hours after adequate lactation had been established. Milk secretion was not interfered with in any way (Fig. 2).

Progesterone.—Because of the difficulty in securing large amounts of this steroid, only 4 patients were studied. Two received 100 mg. in sesame oil intramuscularly over a period of three to four days, respectively, beginning soon after delivery. The onset of adequate milk secretion was not delayed (Fig. 1).

The other two patients received 100 mg. of progesterone intramuscularly in divided doses twenty-four and seventy-two hours, respectively, after lactation had been adequately established. Milk secretion was not suppressed (Fig. 2).

Careful pediatric check-up and follow-up of the babies in the test groups failed to reveal any adverse effects.

DISCUSSION

The process of lactation resolves itself into two fundamental mechanisms: the initiation of milk secretion which is under hormonal control[6] and the maintenance of established lactation which is governed by both hormonal and neurogenic factors.[7] These phenomena must be clearly differentiated from the clinical syndrome of painful engorgement of the breasts. The latter is brought about by lymphatic and vascular stasis, not by distention of the ducts by milk.[8] Failure to differentiate clearly the mechanism by which painful engorgement is brought about from the physiological processes leading to the initiation of milk secretion has led to the confusion apparent in the clinical literature. Although painful engorgement may be associated with the onset of lactation, each is a distinct physiologic entity. Clearly then, the one is not synonymous with the other.

In a previous report, it was pointed out that a sufficient daily dose of estrogen (stilbestrol) would delay the onset of adequate milk secretion in the nursing human being only as long as it was administered.[5] The mechanism of action of stilbestrol was felt to be directly upon the glandular epithelium of the mammary gland, for a cell that is actively proliferating (under the influence of estrogen) cannot secrete at the same time.[9] In other words, the ability of a substance to affect the onset of adequate lactation in the nursing mother seemed to parallel its proliferating influence upon the mammary epithelium. The same conclusion was reached by Folley and Kon[10] in their work on rats.

The reason for the failure of the four steroids studied in these experiments (Fig. 1) to affect the onset of adequate milk secretion in the nursing human being becomes apparent from their relatively slight, if any, proliferative effect upon the mammary epithelium.[11] In fact,

testosterone greatly stimulates the production by the anterior pituitary of lactogenic principle(s),[12] whose release is actively stimulated by the act of suckling.[13] Consequently, the stimulus of a nursing child was more than sufficient to initiate and then maintain adequate lactation.

Milk secretion, once established, is controlled by both hormonal and neurogenic factors.[7] The manner in which the nervous stimulus of suckling is essential for the continued secretion of milk is still not clear.[14] Upon the clarification of this point must await the explanation for the reason why not only massive doses of these four steroids, but also of stilbestrol,[5] have no effect upon established lactation in the nursing human being (Fig. 2).

The mechanism by which painful engorgement of the breasts is relieved by testosterone propionate and methyl testosterone is not as yet known. That it is not by inhibition of lactation is obvious from the results obtained in these studies (Fig. 1). Its fundamental physiology, however, probably involves the ebb and flow of extracellular fluid in some manner. Markee,[15] for instance, has shown that testosterone will bring about a regression in ocular endometrial transplants as evidenced by a decreased amount of fluid in the stroma and by a lessened vascularity.

SUMMARY AND CONCLUSIONS

1. The effects of relatively large doses of testosterone propionate, methyl testosterone, anhydro-oxy-progesterone and progesterone were studied upon the onset of milk secretion and the maintenance of established lactation in the nursing human being.

2. The onset of adequate milk secretion in the nursing human subject was not affected by:

(a) 200 to 300 mg. of testosterone propionate in oil given intramuscularly
(b) 100 to 500 mg. of methyl testosterone orally
(c) 100 to 500 mg. of anhydro-oxy-progesterone orally
(d) 100 mg. of progesterone given intramuscularly

3. Established lactation was adequately maintained in the nursing woman, being unaffected by:

(a) 250 to 500 mg. of testosterone propionate given intramuscularly
(b) 250 to 500 mg. of methyl testosterone orally
(c) 250 to 500 mg. of anhydro-oxy-progesterone orally
(d) 100 mg. of progesterone given intramuscularly

4. The ability of a substance to affect the onset of adequate lactation in the nursing woman seems to parallel its proliferating effect upon the glandular epithelium of the breast.

5. Once lactation is adequately established, however, the stimulus for further milk secretion by the glandular epithelium of the breast, produced by an actively suckling baby, proved to be far stronger than the stimulus to proliferation of this same mammary epithelium, provided by massive doses of not only the four steroids used in this study, but also of the estrogen, stilbestrol.

6. The mechanism by which relief of painful engorgement of the breasts is brought about by testosterone propionate, as well as by methyl

testosterone, does not depend upon inhibition of lactation but probably involves the shifting tides of extracellular fluid.

The author gratefully acknowledges the sincere interest of Drs. Harry Aranow and Milton J. Goodfriend, during the course of these studies. In addition, the splendid cooperation of the Misses Morgan and Newton, of the Nursing Staff of the Obstetrical Division, is deeply appreciated.

Ciba Pharmaceutical Products, Inc., supplied the following steroids: (1) Testosterone propionate under the trade name of Perandren. (2) Methyl testosterone under the trade name of Metandren. (3) Progesterone under the trade name of Luto-cylin. (4) Anhydro-oxy-progesterone.

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THE USE OF TESTOSTERONE PROPIONATE IN THE MANAGEMENT OF PELVIC INFLAMMATORY DISEASE

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IT HAS long been recognized that the menstrual period is a time of danger or flare-up in the course of pelvic inflammatory disease. Most patients with chronic pelvic inflammatory disease suffer from dysmenorrhea and/or menorrhagia. Exacerbations of pelvic inflammatory disease at the time of menstruation are so common that often patients are warned to stay in bed before and during their menses to avoid or lessen the chance of a flare-up. Conversely, few patients who manage to retain their infected tubes until the menopause, require surgery thereafter for the relief of the disease, suggesting that cessation of the menstrual function is beneficial in these patients.

The use of testosterone propionate in treating acute and chronic pelvic inflammatory disease was suggested by the ease with which menstruation can be suppressed by relatively safe doses of androgen.[1] It was hoped that not only could the exacerbations be prevented but that inasmuch as there is a natural tendency for large inflammatory masses to regress and even disappear in well-controlled patients, testosterone propionate might prove to be a helpful adjuvant in the management of this disease.

Beclere[2] employed testosterone propionate for uterine hemorrhages with good results. Mazer (C.) and Mazer (M)[3] used androgen in 38 cases of menstrual disorder, both menorrhagia and metrorrhagia. Greenhill and Freed[4] advocated the use of testosterone propionate in mastopathies, menorrhagia, and dysmenorrhea. Huff-

man[5] suggested the use of androgen therapy in functional uterine bleeding, mastalgias, and puerperal breast engorgement and for the inhibition of lactation and advised further investigation of its use in dysmenorrhea and the treatment of menstrual moliminia. Chiray and Mollard[6] used testosterone acetate in the hope of preventing menstrual flare-ups in women with pulmonary tuberculosis in whom menstruation exerts a harmful influence.

According to Papanicolaou, Ripley and Shorr[7] not only is menstruation suppressed by testosterone propionate but there is produced an atrophic endometrium and an atrophic vaginal smear. Rubin and Davids[8] reported that testosterone propionate has an inhibitory effect on the tubal muscle, diminishing its general tonicity and the amplitude of the contractions. Geist, Salmon, Gaines, and Walter[9] summarize the mechanism of testosterone action as (1) inhibition of the gonadotropic factors of the hypophysis, resulting in failure of ovulation and suppression of the normal formation of estrogen and progesterone; (2) direct inactivation of the available estrogens in the body; and (3) the production of androgenic effects (virilism). Abarbanel[10] has recommended the percutaneous administration of testosterone propionate where this is more convenient, although the dosage required is from three to six times as great as that which is necessary by the subcutaneous route.

In attempting to control and treat pelvic inflammatory disease with testosterone propionate, complete suppression rather than mere reduction in amount and duration of the menstrual flow was sought in the patients treated. The average amount of testosterone propionate per month necessary to suppress menstruation varied in these cases between 350 to 650 mg. The drug was administered in 25 to 50 mg. doses, two to three times per week. The subcutaneous method was employed, as it gives better means of control and observation. Due probably to the use of the sulfonamides, fever therapy, Elliott bag therapy, etc., there appear to be fewer cases of chronic pelvic inflammatory disease available for study. The purpose in reporting so small a series is that other workers may attempt this method of treatment, and its value be better assayed.

CASE REPORTS

CASE 1.—M. H., white, aged 37 years, married, had had chronic pelvic inflammatory disease for at least two years. There had been frequent flare-ups requiring bed rest. Bimanual examination showed right and left tubal masses 4 and 6 cm., respectively. She was treated for four months with total suppression of menstruation. There were no flare-ups during treatment, and there was less pain and disability reported. Pelvic examination at end of treatment showed reduction in size of masses to 3 cm. each adnexa. Periods had not returned two months after end of treatment.

CASE 2.—E. A., white, aged 33 years, married, had acute pelvic inflammatory disease of gonococcal origin. When first seen, she had pelvic peritonitis with fullness of both tuboovarian regions; exact size of masses was at first undefined. Bed rest and analgesics were prescribed, but no sulfonamides were given and testosterone propionate was instituted. Menses were completely suppressed. There was no exacerbation after the first week. At the end of two months, only tubal thickening was palpable. By the third month, no pelvic pathology was palpable. Cervical and urethral smears were negative repeatedly. This case is not included as an example of desired treatment of acute gonococcal infection, but for illustration of effect of testosterone propionate. We would treat any further cases with sulfonamide plus testosterone propionate. Patient was given treatment for four months, but had not resumed flow two months later.

CASE 3.—S. P., white, aged 36 years, single, had chronic pelvic inflammatory disease many years. She had dysmenorrhea and menorrhagia with every period. Pelvic examination showed thickening of left adnexa and a mass 8 cm. in diameter in right side. Menses were completely suppressed. She received complete relief

during the treatment. After four months, pelvic examination showed persistence of thickening of left adnexa but mass in right side was reduced to 4 cm. She was treated for three months with return of flow at fifth month.

CASE 4.—M. M., white, aged 24 years, single, had subacute pelvic inflammatory disease. Recent gonococcal infection was treated with sulfanilamide, but small masses persisted in both tuboovarian regions, which enlarged at last menstrual period. The period was accompanied by dysmenorrhea. There was complete suppression of flow and relief of expected pain. There had been definite reduction of size of masses when the patient was last seen. Treatment was stopped after two months because of voice changes. She had a period at end of fourth month.

CASE 5.—J. T., white, aged 22 years, married, had a gonococcal infection which was treated with sulfanilamide; then conization of cervix was done. A few months later, she had an acute pelvic peritonitis. There was a 5 cm. mass in the left tuboovarian region. The past few periods had been prolonged, painful, and profuse. She was given testosterone propionate and complete suppression of menses was obtained. There were no flare-ups and the mass was reduced to 3 cm. She was treated three months with return of flow at fifth month.

CASE 6.—R. S., white, aged 39 years, single, had a laparotomy five years previously and a left salpingo-oophorectomy for tuboovarian abscess, but she had refused permission for removal of right tube and ovary which were also chronically inflamed. Dysmenorrhea and menorrhagia persisted, though lessened after operation. She was placed on testosterone propionate with complete suppression of menses and almost complete relief of pelvic pain and diminution in size of pelvic mass. She was treated for three months and injections were stopped because of voice changes and hirsutism. Period occurred at end of fifth month.

An analysis of the above cases shows that menstruation was suppressed in all. No flare-ups occurred during the period of observation. In 5 of the 6 cases, there was definite improvement as judged by diminution of the size of the pelvic masses, and in one case, the pelvic mass completely disappeared. It must be borne in mind that these patients were cooperative and under close supervision, and a certain degree of improvement might have been expected in these circumstances with any or no form of treatment. It is not believed, however, that such uniform results would have been attained without the use of the androgen. We believe that testosterone propionate may also be indicated preoperatively in preparation of patients, who flare up, if only slightly, with each menses, and whom we would like to have as quiescent as possible before operation. Being a reversible reaction and automatically permitting the patient to return to normal function merely by ceasing treatment, testosterone propionate would appear to be far more desirable than x-ray therapy, which may produce irreparable change. Caution must be employed, as virilism, although temporary, may be induced by overdosage.

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PREVENTION OF URINARY RETENTION IN THE PUERPERIUM WITH MERCUROCHROME BLADDER INSTILLATIONS

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THE too frequent use of the catheter in a bladder which has become overdistended is acknowledged as a cause for serious urinary tract complications and many methods have been used in an effort to avoid this.

Woodruff and TeLinde[1] reported their experience with prophylactic 0.5% aqueous mercurochrome bladder instillations in a series of gynecologic cases. In their series of 500 laparotomies, there was an incidence of 6.5 per cent of patients with urinary retention, and 0.4 per cent with postoperative pyelitis. In extensive perineal repairs, instillations were reported of little value. Among the recent contributions of significance in connection with physiology and treatment of urinary retention, and pharmacology of the various drugs are the ones by Barber,[2] Moir,[3] Maxwell,[4] Marden and Williamson,[5] Boland,[6] Jordan,[7] Podvinec,[8] and Prather.[9] We have used mercurochrome bladder instillation as a prophylactic measure and in treatment of retention of urine once it has occurred.

At the French Hospital, 2.5 per cent aqueous mercurochrome has been used as bladder instillation immediately following delivery since 1938. The results have been so satisfactory that it has become routine in all clinic deliveries. Any clinic patient not voiding within ten to twelve hours after delivery is catheterized; even sooner if she complains of pain and has a full bladder. We have used intermittent drainage, with catheterization every eight hours for retention. Mercurochrome has been instilled after every third catheterization in these patients. Catheterization for residual urine is used until 50 c.c. or less is obtained.

A study dealing with 500 deliveries followed by routine instillations of 2.5 per cent aqueous mercurochrome is presented. A series of 500 consecutive patients delivered on the private service is reported as control. All patients were delivered in 1940. The study was made on as nearly the normal obstetric patient as possible. For obvious reasons, any patient with ante-partum pyeloureteritis, severe pre-eclampsia, eclampsia, severe cardiac disease, and all premature deliveries (birth weight 5½ pounds or less) is excluded.

TECHNIQUE

The technique for instilling the bladder is simple. It is done immediately after expression of the placenta and completion of the perineal repair, if one is necessary. The urethral meatus is cleaned with lysol solution, a No. 18 French rubber catheter is inserted, and the bladder emptied. A small funnel is then attached to the catheter, through which 30 c.c. of 2.5 per cent aqueous mercurochrome is introduced by gravity.

RESULTS

The data in the 500 deliveries routinely instilled are in Table I.

TABLE I. MERCUROCHROME BLADDER INSTILLATION IMMEDIATELY AFTER DELIVERY

TYPE OF DELIVERY	CASES	RETENTION OF URINE LESS THAN 24 HOURS POST PARTUM	RETENTION OF URINE MORE THAN 24 HOURS POST PARTUM	PYELO-URETERITIS
A. Primiparas:				
Normal spontaneous	128	2	0	1
Low forceps	69	1	1	0
Midforceps	19	1	0	0
Assisted breech	13	0	0	0
Breech extraction	1	0	0	0
B. Multiparas:				
Normal spontaneous	240	1	0	0
Low forceps	14	1	1	1
Midforceps	6	0	0	0
Assisted breech	2	0	0	0
Breech extraction	1	0	0	0
Internal podalic version and breech extraction	2	0	0	0
Spontaneous, twins	1	0	0	0
Operative, twins	4	0	0	0
	500	6	2	2

In the instilled series, 8 patients had retention of urine, 2 of these longer than twenty-four hours post partum. Retention of urine was present in only 1.6 per cent of all deliveries. There was no toxic reaction noted from the mercurochrome instillation. Post-partum pyeloureteritis developed in 2 patients; one of these had urinary retention for longer than twenty-four hours, while the other patient

TABLE II. PRIVATE PATIENTS NOT INSTILLED WITH MERCUROCHROME IMMEDIATELY AFTER DELIVERY

TYPE OF DELIVERY	CASES	RETENTION OF URINE LESS THAN 24 HOURS POST PARTUM	RETENTION OF URINE MORE THAN 24 HOURS POST PARTUM	PYELO-URETERITIS
A. Primiparas:				
Normal spontaneous	100	6	1	2
Low forceps	140	23	7	2
Midforceps	55	6	4	1
Assisted breech	10	1	1	0
Breech extraction	2	0	1	0
Forceps to head in breech	4	2	0	0
Operative, twins	1	0	0	0
B. Multiparas:				
Normal spontaneous	138	5	2	0
Low forceps	29	4	1	0
Midforceps	15	3	0	0
Assisted breech	5	2	0	0
Forceps to head in breech	1	0	0	0
	500	52	17	5

had no use of the catheter, except for diagnostic urine culture. Both cases of urinary infection were proved by positive urine culture. The morbidity in the 500 deliveries was 5.8 per cent (100.4° F. used as standard). The one-day fevers

were 4.2 per cent. There were 5 prolonged labors (thirty hours or more), and 36 short labors (three hours or less). The total operative incidence was 26.2 per cent. Three third-degree lacerations were repaired.

RESULTS

The data on the private patients who had no bladder instillation immediately following the delivery are tabulated in Table II.

There were 52 patients among the private patients with retention of urine, who required catheterization one or more times in the first 24 hours post partum. Seventeen patients had serious retention of urine for longer than twenty-four hours. The total percentage of patients having urinary retention was 13.8 per

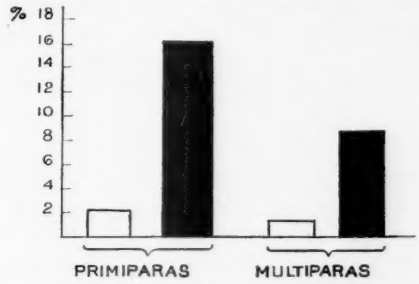

Fig. 1.—Percentage of patients with retention of urine.

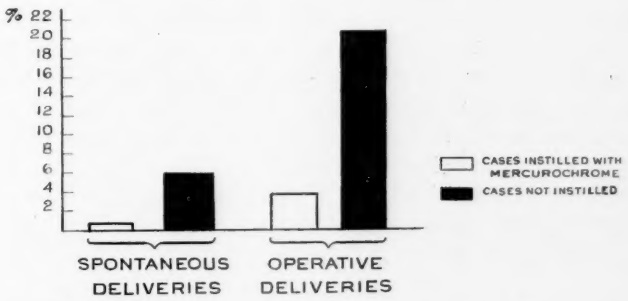

Fig. 2.—Percentage of patients with retention of urine.

cent. Randall and Murray[10] report 15 per cent of puerperal women require catheterization. It is noteworthy that 5 patients developed post-partum pyelo-ureteritis, 4 of these having urinary retention before signs and symptoms of urinary tract infection became evident. One of the patients catheterized for longer than twenty-four hours developed pollakiuria. The morbidity was 3.4 per cent in this series while the one-day fevers were 6.4 per cent. The operative incidence totaled 52.4 per cent. There were 14 short labors and 11 prolonged labors. One third-degree laceration was repaired.

Fig. 1 shows the percentage of cases in both series of 500 deliveries divided according to parity. The spontaneous and operative deliveries in which the catheter was used for retention of urine in the puerperium is illustrated in Fig. 2. It is well shown in the charts that primiparity associated with operative delivery was by far the most frequent case to develop post-partum retention of urine. In more than half of the primiparas with retention of urine, the duration of labor was more than twenty hours. Randall and Murray[10] emphasize the highest percentage of puerperal urinary retention in the longer labors.

Orders for post-partum catheterization in the private cases varied from eight to eighteen hours. After retention of urine had developed in 14 private cases, a 30

c.c. bladder instillation of 2.5 per cent aqueous mercurochrome was given. However, in two of these patients with an overdistended bladder treated in this manner untoward urinary symptoms developed. One patient had hematuria for three days, and the other had pollakiuria which lasted five days. It seems the overdistended bladder mucosa is more sensitive to the mercurochrome and is more likely to toxic reaction.

In the instilled series of cases, it was a fairly common occurrence for the patient to void involuntarily while still under the effect of analgesic drugs. The use of morphine, pentobarbital and scopolamine apparently had no effect on the retention of urine in the instilled series. The type of anesthesia in all the cases, except those delivered with procaine pudendal block and local perineal infiltration, was nitrous oxide-oxygen mixture, supplemented by ether in a closed system. No attempt was made to evaluate the effect of anesthesia on urinary retention. There were no bladder injuries in either series of cases. Dührssen's incision in the cervix was not done. However, 3 cases required suturing of a cervical laceration after delivery. The repairing of an episiotomy or perineal laceration apparently had no relation to retention of urine. All patients had pelves ample for full-term deliveries per vaginam.

SUMMARY AND CONCLUSIONS

1. Aqueous solution of mercurochrome for bladder instillations as the prophylactic preventive and treatment of retention of urine in the puerperium is outlined.

2. Of the cases in the instilled series, 1.6 per cent and, of the cases in the control series, 13.8 per cent had puerperal retention of urine. This is approximately a 9 to 1 difference.

3. Post-partum pyeloureteritis was a complication in 0.4 per cent of the routinely instilled patients, and 1.0 per cent of the control series.

4. Frequent bladder catheterization in the presence of retention of urine was an important cause of post-partum pyeloureteritis.

5. Primiparas in whom operative deliveries were done were the most frequent patients to develop retention of urine.

6. The repair of an episiotomy or perineal laceration had no relation to retention of urine in the puerperium.

7. The incidence of urinary retention was related to the duration of the labor.

8. No correlation was found between retention of urine and the use of analgesic drugs.

9. No toxic effects were noted from the mercurochrome in the instilled series of patients.

10. Sensitivity to the mercurochrome was observed in the overdistended bladder. Mercurochrome should be used with caution in these patients.

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PROLAPSE OF THE UTERUS DURING PREGNANCY

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PREGNANCY associated with marked prolapse of the uterus is rare; only one such case has been observed among more than thirteen thousand obstetric admissions at the University Hospital between January, 1926, and July, 1940. At the Wisconsin General Hospital* there was a similar case among two thousand admissions between Jan. 1, 1930, and Jan. 1, 1940, the patient having had four pregnancies since the onset of the procidentia. The third case† was reported by a private practitioner in Wisconsin.

CASE 1.—V. M. (Hosp. No. 40-1081), a 28-year-old, married, white secundigravida, was admitted to the University Hospital, Iowa City, Jan. 24, 1940. The last menstrual period began May 16, 1939, making the expected date of delivery Feb. 23, 1940.

The patient had developed a band type of scleroderma with muscular atrophy at the age of eight years. The skin changes were distributed irregularly over the face, trunk, and extremities. The first pregnancy had ended in a normal, spontaneous delivery in 1934. Several months later a persistent incomplete prolapse of the uterus was noted.

During the first months of this second pregnancy, there were no complaints, but six weeks prior to admission the cervix rapidly became larger and longer, and there was daily "spotting." Later the organ attained such a size and protruded so far beyond the introitus that walking was difficult.

On admission the cervix, which was hypertrophied and elongated, protruded 10 cm. beyond the introitus; it was cone-shaped with the largest diameter about the external os, at which level the circumference was 22 cm., while at the introitus it was 15 cm.; there was marked erosion and ulceration about the external os from which hung a small mucous polyp. The uterus extended to within 6 cm. of the xiphoid; the fetus was in R.O.A. position, and the fetal heart was audible in the right lower quadrant; there was no evidence of pelvic disproportion.

Course in the Hospital.—Bed rest in slight Trendelenberg position with a heat cradle over the body was prescribed. Warm glycerin packs, containing 5 per cent mercurochrome, were applied to the cervix for one-half hour three times daily. As the size of the cervix diminished, it was pushed gently into the vagina, which was packed lightly. However, it was never possible to prevent recurrence of the prolapse for more than twenty-four hours. The erosion healed gradually. Despite the fact that the fetal head was engaged and the baby seemed of mature size, the patient had not gone into labor by March 1. On that day and again on March 6 unsuccessful attempts were made to induce labor medically. On March 11, 500,000 international units of progynon B in oil were given intramuscularly. Twenty-four hours later labor began spontaneous.

After ten hours in the first stage of labor, which had progressed normally, the head was on the pelvic floor and the scalp was visible. The cervix was dilated 4 to 5 cm. and well effaced. At this point labor stopped and for the next twelve hours there was no progress. It was then decided to effect delivery by cervical incisions and forceps. The baby was a normal male weighing 3,255 Gm.

*This case report was made available through the courtesy of Dr. J. W. Harris, University of Wisconsin Medical School, Madison, Wisconsin.

†This case report was made available through the courtesy of Dr. F. A. Wendt, Johnson Creek, Wisconsin.

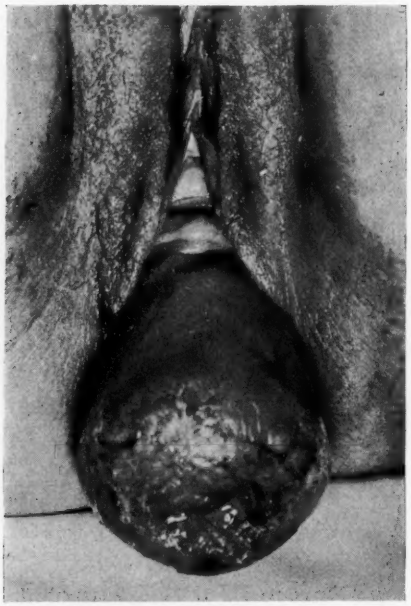

Fig. 1.—Case 1. Appearance of prolapse on admission showing ulceration, edema, and hypertrophy.

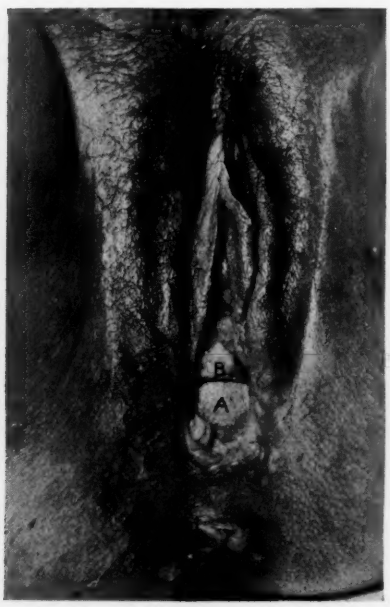

Fig. 2.

Fig. 3.

Fig. 2.—Case 1. In labor, station of head just before Dührssen's incisions were made. *A*, Fetal scalp; *B*, anterior lip of cervix.

Fig. 3.—Case 1. Appearance of the cervix at time of discharge. *A*, *B*, *C*, healed Dührssen's incisions.

The puerperium was afebrile and uncomplicated except for a right Bell's palsy which developed on the third day after delivery. At the time of discharge on the thirteenth day the cervix protruded 1 cm. beyond the introitus, and the incisions were well healed.

Follow-up.—The patient returned to the Hospital June 4, 1940. There was no complaint except the prolapse. The cervix protruded 2 to 3 cm. beyond the introitus and could be pulled out that much farther. The Dührssen's incisions were scarcely visible. The uterus was retroverted and enlarged slightly. Both adnexa were free. The facial palsy had disappeared completely. Vaginal hysterectomy and plastic repair were done on June 7. Pathologic examination showed hyperplasia of the endometrium and uterine endometriosis. The postoperative course was satisfactory and the patient was discharged June 17.

CASE 2.—J. R. (Hosp. No. 35280), a 26-year-old, married, white, octipara, was first admitted to the Wisconsin General Hospital in 1928. At that time she indicated she had had a normal delivery in 1925 and twins in 1927 with no complications. In 1928, her first admission to Wisconsin General Hospital, a hydrocephalic monster was delivered after craniotomy. No mention was made at this time of any relaxation of the vaginal outlet. The fourth gestation, in 1929, was associated with a marginal placenta previa; a living child was obtained by version and extraction. Incomplete procidentia appeared in the second week of this puerperium.

During the next seven years the patient had four more deliveries, January, 1932, May, 1934, June, 1935, and April, 1937. With each of these later pregnancies, there was marked uterine prolapse, and signs of threatened abortion appeared during the gestation period in 1932.

The cervix which often protruded beyond the introitus was hypertrophied, eroded, and badly lacerated. At each delivery, the fetal head could be seen through the dilating cervix. The labors were normal and the deliveries were spontaneous. The uterus was packed after one delivery to control bleeding, and at the time of the last confinement there was a severe post-partum hemorrhage due to uterine inertia, and the fact that it was not possible to massage the fundus. All puerperiums were afebrile. The babies were normal, weighing more than 2,500 Gm. each at birth. After each of the last four deliveries, surgical repair and sterilization were recommended, but were refused because of religious convictions.

CASE 3.—K. W., a 43-year-old, married, white, secundipara, was first seen Dec. 1, 1939. The two previous deliveries had been uncomplicated. The prolapse was first noticed in 1937 and had gradually increased. The patient was in good physical condition, the only positive findings were a four and one-half months' pregnancy associated with marked prolapse. The cervix which protruded 6 cm. beyond the introitus was edematous and partially ulcerated. During the next few weeks the patient's activity was limited. After the seventh month complete bed rest was ordered. During the period of rest the ulceration and edema almost entirely disappeared under local applications of silver nitrate.

The patient was hospitalized immediately at the onset of labor. Dr. Wendt's comment on the course of labor was "Watchful waiting was the main item in this delivery and I never felt it necessary to be radical and do a section. It was interesting to watch the progress as the cervix was completely outside the introitus and one could watch the dilation which was slower than usual, until pressure was applied to the cervix to hold it back in the canal." The child then was delivered by low forceps. The baby was normal and the puerperium was uneventful. Several months later a total hysterectomy and plastic repair were performed.

LITERATURE

Based upon the number of cases reported, it is apparent that prolapse of the uterus associated with pregnancy is unusual. Most of the recorded cases that have gone to term showed only an elongated, hypertrophied and edematous cervix. The first and third cases above are of this type. Complete procidentia is hardly compatible with a full-term gestation.

TABLE I. SUMMARY OF 170 CASES OF UTERINE PROLAPSE DURING PREGNANCY

SOURCE	YEAR	TOTAL NO. OF CASES	CASES WITH DATA	OPERATION DURING PREGNANCY	ABORTIONS	SPONTANEOUS DELIVERIES	FORCEPS	VERSIONS	DÜHRSSEN'S INCISIONS	CRANIOTOMIES	CESAREAN SECTION	FETAL DEATHS	MATERNAL DEATHS
1. Franke	1892	124	116	6 plastic repairs	20	51	29	6	34	10		26	5
2. Seitz, Ludwig	1901	9	Included in above										
3. Andrews, H. C.	1906	4	4	1 plastic repair		3	1		1			1	1
4. Findley, Palmer	1911	10	3		1 therapeutic abortion (with plastic repair)		2		2			1	
5. Hertzler, A. E.	1911	1	1			1							
6. Dorsett, W. B.	1911	1	1			1							
7. Harris, J. C.	1912	1	1		1 therapeutic abortion								
8. Solomons, B.	1912	2	2	1 plastic repair	1	1							
9. Barton	1912	1	1 (Partial data)									1	1
10. Kennedy	1912	1	1 (Partial data)									1	1
11. Maurizia, B.	1912	1	1			1							
12. Faivre	1918	1	1				1						
13. Maxwell, J. C.	1925	4	4				3		3	1		1	1
14. Williams, J. W.	1930	1											
15. DeLee, J. B.	1933	3											
16. Higgins, D. E.	1934	1	1								1		
17. Serbin, W. B.	1934	2	2			2							
18. Keettel, W. C.	1940	3	3			4*	2		1				
Totals		170	142 (140 complete data)	8	23	64	38	6	41	11	1	31	9

*One patient delivered 4 times.

However, cases have been observed that went to the seventh lunar month with the uterus outside the body before delivery occurred.

The *Index Medicus* revealed 170 reported cases of pregnancy associated with more or less complete uterine prolapse, 137 of which were collected before 1901 by Franke,[7] Seitz,[14] and Andrews.[1] Palmer Findley,[6] in 1911, made the last review and added 10 cases. Twenty-three other reports have appeared in the interval, including the 3 here reported. Clinical data were available in 142 of the 170 cases, with complete data on 140.

Parity.—Among the 170 recorded cases, there were 19 primigravidas, 82 multigravidas, and 69 individuals on whom no data were available. Trauma was cited as the most frequent cause of prolapse among the primigravidas.

Complications of Pregnancy.—The majority of these women had been aware of the prolapse before conception. Many authorities offered the comment that fertility was not altered. The second individual recorded here illustrates this point, since she had become pregnant four times following the onset of the procidentia. In several instances prolapse developed after the onset of the pregnancy, and Maxwell[13] feels that such an occurrence can be attributed to sudden trauma or straining. Many patients were reported as uncomfortable and even bedridden because of the protruding mass.

Among the 140 cases with adequate clinical data, there were 21 spontaneous abortions, or 15 per cent. There is no definite explanation for this high incidence of abortion, except that it may be due to temperature changes and trauma. There were only two therapeutic abortions, or 1.4 per cent; one was accomplished by vaginal hysterotomy, combined with anterior and posterior wall repair and cervical amputation; the other was terminated by total hysterectomy at the fifth month.

Eight, or 5.7 per cent, had either anterior and posterior wall repairs or cervical amputations between the second and fifth months of pregnancy. None of these patients aborted and all were delivered spontaneously.

Delivery.—Delivery was normal in 64, or 45.7 per cent, of the cases; 38, or 27.1 per cent, were delivered by forceps, mostly low applications following Dührssen's incisions. Eight fetal deaths occurred in this group. Dührssen's incisions were employed 41 times, or in 29.3 per cent of the total. The infants were usually extracted by forceps, but on several occasions spontaneous delivery occurred. Faivre[5] reported one case where the assistant pushed the cervix back over the baby's head so that the delivery occurred normally; Case 3 also demonstrated this procedure.

Delivery was effected six times, 4.3 per cent, by version and extraction with two fetal deaths. Craniotomy was done 11 times, 7.8 per cent, including 3 operations involving living fetuses. Ten of the craniotomies were reported by Franke[7] and Seitz.[14] Cesarean section was performed once; the operation was of the Porro type with fixation of the cervical stump. Harris[8] advocated that every woman with prolapse should have this type of treatment.

Fetal Deaths.—Thirty-one babies died during, or immediately after, delivery, making a fetal death rate of 22.1 per cent. While it was impossible to compile accurate data, it was noted that premature delivery was frequent.

Maternal Morbidity and Mortality.—Morbidity data were available on only 112 and mortality data on 142 women. Fourteen were grossly infected, an incidence of 12.5 per cent. There were 9 maternal deaths, or 6.3 per cent. One death was due to perforation of the uterus and eight to infection.

COMMENT

Prolapse of the uterus is rightly considered a serious complication of pregnancy. The condition apparently has little effect upon fertility, and pregnancy frequently occurs in spite of marked chronic cervicitis. Early abortion is relatively frequent. Therapeutic abortion has been seriously advocated, and Findley,[6] in 1911, recommended interruption of the pregnancy followed by plastic repair, provided the patient were incapacitated during the early part of pregnancy and showed no improvement following bed rest. Later upon learning of the work of

Seitz[14] he was of the opinion that repair should be done without interruption of the pregnancy.

Patients who did not abort frequently improved after the fourth or fifth month of pregnancy, because the uterus rose out of the pelvis pulling the cervix into the vagina. Among the earlier cases Franke,[7] Seitz,[14] and Maurizia[12] all recommended a pessary to hold the cervix in the vagina during the early months of gestation with removal of the appliance as the uterus enlarged and the cervix was drawn upward. Seitz[14] even advised anesthetization of the patient and replacement of the uterus with insertion of a pessary regardless of the duration of the pregnancy.

It was felt by Andrews[1] that the incidence of breech presentation was increased, but he offered no statistical evidence to support his opinion.

The operative incidence was extremely high in the reported cases. The most common method of delivery, excluding spontaneous expulsion, and perhaps the safest operative procedure were the use of forceps after Dührssen's incisions, which are easily made with the cervix presenting. Exposure is excellent and the cervix is usually well effaced. Version and extraction, craniotomy, and cesarean section were used only occasionally.

The fetal death rate was high. This was largely explained by the need for operative intervention, the prolonged labors, and the number of premature infants.

Among the 14 cases of maternal sepsis there were 8 deaths (57.1 per cent). The number of severe infections was not great considering the operative incidence, the prolongation of labor, and the fact that delivery was made through a potentially infected field. Before 1911, when puerperal infections were more common, there were 6 deaths in 120 cases, a mortality rate of 5 per cent; yet from 1911 to 1940 there were 3 deaths in 22 cases, a death rate of 13.6 per cent.

SUMMARY

Three women having prolapse of the uterus associated with pregnancy are presented. One hundred and sixty-seven other reports have been collected from the literature. The outstanding features associated with this complication are the frequency of abortion, the high operative incidence to effect delivery, and the high percentage of fetal and maternal deaths. The treatment was formerly radical, but in recent years has been conservative. Aside from spontaneous expulsion, which is frequently possible, the simplest and safest method of delivery is low forceps following Dührssen's incisions.

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UTEROLIGAMENTOPEXY OPERATION FOR RETROVERSION OF THE UTERUS (NONPUERPERAL)

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THE development of a surgical method for the satisfactory correction of retroversion of the uterus, especially during the childbearing period, has been a perennial challenge to the ingenuity of gynecologists. As a consequence various methods have been devised, from time to time, and their results have been not infrequently disappointing, having, among other shortcomings, 4 to 15 per cent recurrences.

Forty-one per cent of uterine retroversions are represented by the puerperal type which, although most symptomatic, is likewise the most remediable through the early use of nonsurgical measures, such as the knee-chest position, monkey walk, or the Smith-Hodge pessary.

On the other hand, asymptomatic retroversion allowed to continue uncorrected is destined to prejudice the well-being of women who menstruate by (1) pressure symptoms, (2) uterine adhesions conducive of abortion, (3) twisting of the tubes and the pointing of the portio vaginalis favoring infertility, (4) chronic passive congestion of the uterus followed by myometrial replacement with fibrous tissue, producing a menorrhagia progressive and from which effective relief is obtainable only by hysterectomy, bilateral oophorectomy, or x-ray menostasis with inevitable and unpredictable consequences. The early correction of this type of retroversion would inaugurate a prophylactic policy productive of gratifying returns in the preservation and promotion of functions involved.

It is the symptomatic type with no menorrhagia, however, with which we are chiefly concerned.

It might not be amiss, here, to make a critical review with comments on a few of the prevalent methods employed.

The Alexander operation, in addition to being a rather blind procedure and depending for support solely on use of the weaker portion of the round ligaments, is totally unsuited in cases with complicating adhesions or large fibroids. This operation has a recurrence of 15 per cent. The "internal Alexander operation" is an improvement.

While in the Gilliam operation the stronger portion of the round ligaments is attached to the fascia of the abdominal wall, it is attached indirectly also to the sensitive parietal peritoneum and at the same time creates an opening through which a loop of gut could become incarcerated and even strangulated. Simpson's modification of this operation offers some improvement.

The Ferguson operation, also, causes an indirect attachment of the round ligaments to the parietal peritoneum and, besides, renders these ligaments extra-abdominal structures.

The Coffey operation, an imbrication of the upper and stronger portion of the round ligaments across the anterior uterine wall, utilizes likewise only the round ligaments, fibromuscular structures, for support.

The Baldy-Webster operation, by suturing the round ligaments brought through the broad ligaments to the posterior uterine wall, distorts the normal relationship of the round ligaments to the uterus and broad ligaments and, at the same time employs the weaker portion of the round ligaments for support. This operation is not suited for a heavy uterus.

The Olshausen operation makes use of the stronger portion of the round ligaments and raises the pivotal point of the uterus; but by suturing these ligaments to the parietal peritoneum and causing the uterus to suspend indirectly therefrom, it, likewise, distorts the normal relationships of these ligaments, the uterus, and involved peritoneum.

The Bissell operation, by the intraligamentous shortening of the broad ligaments, also raises the pivotal point of the uterus, an ideal procedure for slight uterine descent. It depends upon section and duplication of the round ligaments for maintenance of the corrected retroversion. This operation is technically difficult, time-consuming, and has a recurrence of 4 per cent.

The fact of the prevalence of so many methods for the treatment of retroversion is evidence that none of these operations has met adequately the major requirements for ultimate satisfactory results, generally.

Hence, a method anatomically sound, physiologically planned, free of the shortcomings of former methods and having a percentage recurrence less than that of former methods seemed timely and desirable. Such is the nature of the method developed and about to be described based on the treatment of 300 cases of uterine retroversion in our service during the past fifteen years with a recurrence of only 2 per cent. It is with the view that the successful employment of this operation, by others, for the correction of the types of nonpuerperal retroversion, designated above, may warrant widespread acceptance that this report is presented.

THE UTEROLIGAMENTOPEXY OPERATION

Due credit must be given to Dougall Bissell, the first to trace, by dissection, the thin layer of subperitoneal abdominal fascia into the uterine ligaments.

Initiation of this operation was based on the recognition of that fact; and its possible development was predicated on knowledge that the utilization of fascia would be as fundamentally essential to ultimate support and satisfaction, here, as it is for a successful hernial operation or other gynoplastic technology.

TECHNIQUE

The usual midline or paramedian incision is made sufficiently long to admit freely one hand into the abdominal cavity. The uterus, tubes and ovaries are sought and freed of any complicating adhesions and/or fibroids. The fundus of the uterus is then brought forward manually to a point that parallels its body with the direction of the pubic symphysis. Care is taken not to anteflex the uterus, for, by so doing, the line of force of intra-abdominal pressure in the erect position would be directed against the posterior wall of the uterine body, producing eventually pathologic anteflexion, a condition less desirable. By placing the uterus as stated above in the erect position, the abdominal pressure is directed against the posterior half of the uterine fundus, forcing the latter slightly forward (anteflexion) against the pubic arch which absorbs this force and prevents uterine descent.

With the fundus so placed, slack is created in the round ligaments and the anterior fold of each broad ligament. Maintenance of the fundus in this corrected position and taking-up this slack are effected by the attachments of three calculated points, roughened or denuded of serosa on the anterior fold of each broad

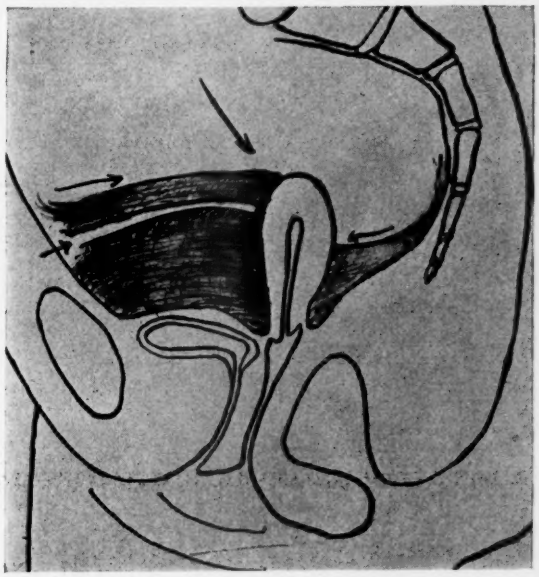

Fig. 1.—Retroverted uterus showing broad, round, and uterosacral ligaments stretched and showing direction of intra-abdominal pressure against anterior surface of fundus uteri.

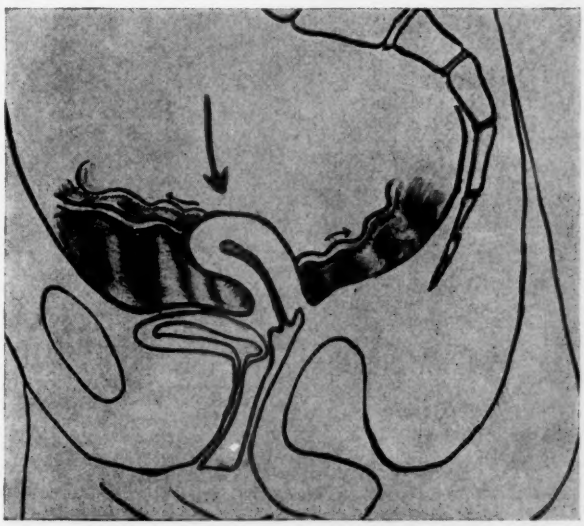

Fig. 2.—Uterus corrected, showing slack in ligaments and direction of intra-abdominal pressure against posterior surface of fundus uteri.

ligament, to corresponding roughened points on the anterior surface of the uterus by use of four No. 5 braided silk and two No. 2 chromic catgut sutures, as follows: Each silk suture in a round needle is started at a point on either side of the round ligaments with a generous bite of broad ligament tissue, including the subjacent

fascia at a distance sufficient from the uterus and ends with a similar bite through the corresponding point on the uterus lateral to the origin of the respective round ligament. Similarly, each catgut suture starts on the broad ligament with a bite including the depth of the round ligament and, after two or three such bites, ends with a deep bite at the point on the uterus between and slightly above the attachments of the silk sutures.

Fig. 3.—Showing placement of sutures in broad and round ligaments.

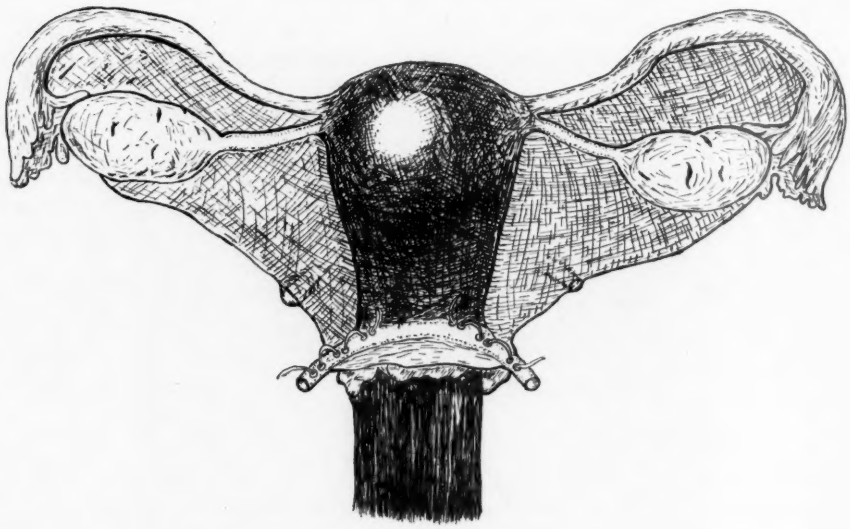

Fig. 4.—Showing sutures in uterosacral ligaments.

The corrected uterus is thus fortified with six new points of fascial attachments rendering the operation anatomically constructed and physiologically designed to insure ultimate therapeutic effectiveness.

Changing the fundus from the retroverted position shifts, concomitantly, the pointing of the portio slightly dorsad, producing corresponding slack in the uterosacral ligaments. This slack is taken up with a deep gathering stitch of heavy

black silk in each ligament, causing slight anteversion, thereby rendering impossible a pathologic anteflexion; and by maintaining the portio within the environs of the receptaculum seminis, the normal or ideal position of the uterus is obtained.

A correspondingly higher attachment of the uterovesical fold of peritoneum to the body of the uterus with a running stitch of No. 1 chromic catgut augments the success of the operation and improves the support of the bladder. At the same time, correction of the accompanying prolapsed ovaries adds materially to the convenience and comfort of these women.

Our experience from the use of this operation warrants the conclusion that a retroverted uterus, so corrected, is ideally posed for the continuance of normal menstruation, for withstanding securely the force of intra-abdominal pressure, and for effecting normal and, more likely, a fruitful insemination.

SUMMARY

1. The successful treatment of 300 consecutive cases of retroversion of the uterus (nonpuerperal) by an uteroligamentopexy operation is described.

2. Various methods for the treatment of such retroversions with their shortcomings, including 4 to 15 per cent recurrences, have been reviewed.

3. This operation has for its intrinsic appeal simplicity of performance, anatomic soundness, physiologic adaptation, maintenance of normal relationships of the uterus and its ligaments to surrounding structures, recurrence of only 2 per cent and results ultimately satisfactory.

4. The timely correction of retroversion of the uterus (asymptomatic) in women who menstruate is recommended as a policy rational and prophylactic.

5. Use of this operation is commended to the profession with the hope that the resultant satisfaction may merit its increasing recognition.

Pennell, Vernon: Removal of a Teratomatous "Twin," Brit. M. J. 2: 414, 1940.

A 6 by 4 by 3.5 inch lower lumbar and sacral mass was removed from a 5-week-old female. The mass had caused no difficulty at delivery. The mass was dissected free from the child under local anesthesia. A meningocele was found in the mass, this was opened, dissected free, and sutured. The child recovered in good condition. The mass consisted of much fat and connective tissue in addition to: (A) A smooth 2 by 1.5 inch cavity lined by cartilage or bone, containing: (1) A stomach which was connected to 7 inches of intestine leading to a blind cecum. (2) Two small buds, possibly liver and pancreas. (B) A tube (? esophagus) leading from the stomach to an external dimple on the mass. (C) Two small protuberances, possibly mandibular processes. All 3 layers were represented.

FRED L. ADAIR AND LESTER CRISMON.

HUMAN THORACOPAGUS MONSTER (SO-CALLED SIAMESE TWINS)

Case Report and Anatomical Study

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HUMAN fetal monsters are rare, and it is, therefore, an exceptional opportunity to be able to examine a full-term double monster in detail. Interest in double monsters has been recently stimulated by the re-publication of the autopsy report of the original Siamese twins.[1] The case we are reporting is of especial interest, because it is only the second of its kind in a total of 82,000 deliveries at the Cook County Hospital since 1905. Ysander[2] in his monograph states that there were 226 known cases of thoracopagus tetrabrachius tetrapus reported in the literature up to 1911. His search through 1922 added 42 more cases, bringing the total to 268. We have found 63 additional cases, including our own, reported since that time to date, increasing the total to 331.

Mrs. E. K., white, aged, 39 years, gravida iii, para ii, entered Cook County Hospital at 5:50 P.M. on July 29, 1940, in labor, having moderate pains every four minutes. She had had two previous normal full-term pregnancies, delivered at home. There was a history of twins on both sides of her family.

Physical examination showed the patient to be in good condition. Her blood pressure was 116/80, and the urine was negative for albumin. The blood Wassermann test was negative, and the smears negative for gonococci.

Rectal examination revealed the cervix about 5 cm. dilated with fetal membranes intact and the presenting part at a one-plus station. Fetal heart tones were regular at a rate of 140.

The patient's last menstrual period was Oct. 13, 1939. Her previous labors had been normal with uneventful recovery. She was now having moderate pains every four minutes and was making good progress. At 7:50 P.M., two hours after admission, the membranes were bulging at the introitus and were ruptured. At this time twins were not suspected. At 8:30 P.M. the first twin was delivered but hung at the outlet. Vaginal examination revealed a second fetus in a transverse position, joined to the first by a stalk attached to the sternum. The union had been along the thorax, sternum, and lower abdomen, but most of this union had been sundered during the delivery of the first twin. There was complete evisceration of the liver and intestines. The stalk was severed and a version and extraction was done on the second twin. Both fetuses were stillborn. Because of hemorrhage, the placenta was removed manually. The placenta was single with one umbilical cord.

The patient was given 1 c.c. of pituitrin intramuscularly and 1 c.c. of ergotrate intravenously and had an uneventful puerperium, leaving the hospital on the ninth post-partum day.

Necropsy Findings.—(J. D. K.) The general form and contour of the monster are shown in Fig. 1. The relationship of the skeletal structures appeared normal as seen in an x-ray plate (Fig. 2). The twins were normally developed males externally; the larger (No. 1) weighed 2,250 Gm. and was 47½ cm. long; the smaller (No. 2) weighed 2,100 Gm. and was the same length. Each had normally developed upper and lower extremities. The scrotal sac of Twin 1 was empty, while that of Twin 2 contained the left testicle only.

The line of fusion of the twins began at the levels of the fourth rib of Twin 1 and the third rib of Twin 2. All the layers of tissue from the skin to the costal cartilage were involved at the upper end of the fusion, there being a common

xiphoid. The skin ended about 1 cm. below the umbilicus and the remainder of the union was by a common peritoneal sac into which the liver bulged.

When the twins were separated, the defects formed were roughly oval shaped and measured 10.5 cm. in length and 11 cm. in greatest transverse diameter. In Twin 1 the manubrium appeared normal and the defect exposed the lower end of the body of the sternum, the xiphoid, and the ribs on both sides. The diaphragm was at the level of the sixth rib and had been fused to the diaphragm of the mate. In Twin 2 the defect commenced at the third rib. The sternum lacked a xiphoid process exposing the thoracic cavity. The diaphragm was likewise at the level of the sixth rib.

Fig. 1.—Photograph of the twins following birth. Note protrusion of large liver.

The organs of Twin 1 were, in general, better developed; most of the fused heart and most of the liver were present in this twin. Only those organs showing abnormalities will be described in detail.

A thymus gland was present, overlying the heart. There was a common pericardial sac and the hearts, which were each composed of three chambers, were fused to form a common circulation (Figs. 3 and 4). The heart of Twin 1 consisted of two large ventricles, the right larger than the left, and a single large auricle. The walls of the ventricles were hypertrophied. There was a widely patent tricuspid valve and a large interventricular septum defect. The superior and inferior venae cavae emptied normally into the auricle. There was a transposition of the large vessels with the aorta, arising from the right ventricle and the pulmonary artery arising from the left ventricle posterior to the aorta. The pulmonary ostium was stenosed. There was no ductus arteriosus. The vessels arising from the arch of the aorta showed no abnormalities. The mitral valve was missing.

Originating from the inferior aspect of the left ventricle close to the apex were the two rudimentary ventricles of Twin 2. These ventricles communicated with one another through a small defect and were attached to a common auricle by a fibrous cord. This common auricle had only a vestigial septum. The superior and inferior venae cavae entered the right half of the auricle. There was present also a similar transposition of the large vessels. The pulmonary ostium was stenosed. The left subclavian and common carotid arteries originated from a common short trunk. There was no ductus arteriosus.

There were two separate respiratory systems, the lungs of Twin 2 were three-lobed, and were half the size of those of its mate. Practically all of the liver was in Twin 1, except for a rudimentary lobe in the other to which it was attached.

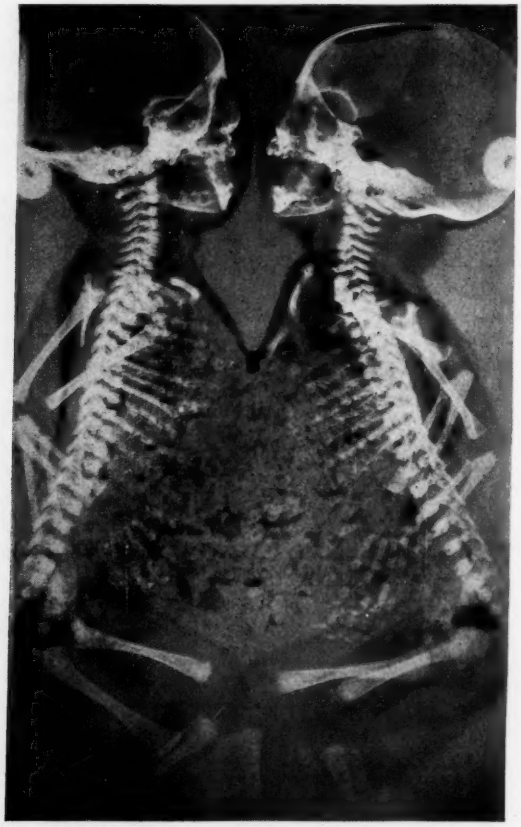

Fig. 2.—Photograph of the x-ray showing the normal skeletal structure.

There was only one system of gall bladder and extrahepatic bile ducts. There were two pancreatic ducts. The gastrointestinal tracts were normal in both; spleens, pancreases and adrenals were normal. A single left testicle of Twin 1 was in the abdominal cavity; Twin 2 had two testicles, an abdominal testicle on the right, the other descended into the left half of the scrotum. The kidneys, ureters and urinary bladders were essentially normal in Twin 1, but in the second twin these organs presented some interesting anomalies which will be described in detail.

The kidneys were markedly reduced in size; the right one measured 18 by 18 by 5 mm. and the left one measured 26 by 12 by 13 mm. The right kidney, upon sectioning, contained a narrow rim of parenchyma up to 1 mm. in thickness. There was a marked dilatation of the renal pelvis and calyces, the pelvis being up to 26 mm. in circumference. In the right ureter the proximal 16 mm. was dilated up to 15 mm. and narrowed downward to a 2 mm. opening which extended into a huge

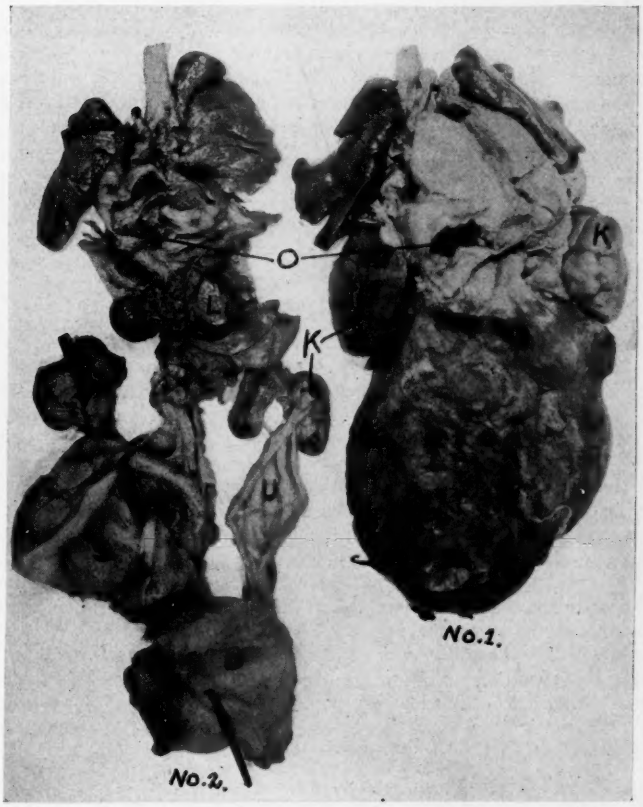

Fig. 3.—Photograph of the organs of both twins. *O*, shows the site of the fusion of both hearts; *L*, liver; *K*, kidneys; *S*, saccular outpouching of the right ureter; *B*, urinary bladder; *U*, megaloureter.

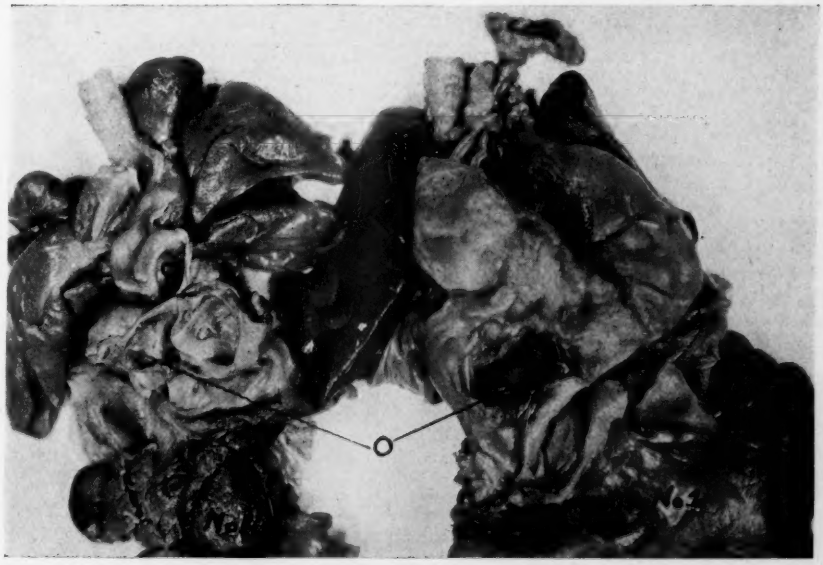

Fig. 4.—Photograph to show close-up view of the hearts of the twins. *O*, site of fusion of both hearts. Note the marked hypertrophy (*H*) of the ventricles in No. 1. *C*, the fibrous cord between the ventricles and the large auricle.

sac 65 mm. in length and 43 mm. in transverse diameter. This sac, which occupied the middle two-thirds of the ureter, communicated with the distal end of the ureter through a small 1 mm. opening. The distal end of the ureter was 32 mm. long and was dilated up to 12 mm. in circumference. The ureterovesical orifice was patent. The left kidney contained more parenchyma than the right, and a cortex and medulla were distinguishable. The left ureter was 95 mm. long and its upper third was markedly dilated up to 31 mm. in circumference; near the distal end the circumference was reduced to 6 mm. The ureterovesical orifice was patent. The urinary bladder was dilated (Fig. 3).

No examination of the central nervous system was made.

SUMMARY

A case of a thoracopagus monster is presented, consisting of two male fetuses united at the thorax and upper abdomen. The union extended from the manubrium to about 1 cm. below the umbilicus. The common thorax contained 4 pleural cavities, a thymus, a single pericardium and a conjoined heart. A common diaphragm separated the thoracic structures from a single peritoneal cavity. There was a large fused liver with an additional rudimentary lobe, one gall bladder, and one system of bile ducts. The gastrointestinal tracts were normal. There were 3 testicles, 2 in the abdomen and 1 in the scrotum. The urinary tract of one twin presented several anomalies, namely a saccular dilatation of one ureter, with a megaloureter on the other side, and a marked hypoplasia of the kidneys. The two pulmonary systems presented no anomalies other than the small size and the presence of three lobes in each lung of one twin. The embryologic defects in the cardiovascular system were very pronounced. The hearts, one better developed than the other, consisted of 3 chambers each and were fused to form a common circulation. There was a transposition of the large vessels. The single umbilical cord attached to a common placenta contained 6 vessels, 2 umbilical veins and 4 arteries, normal in origin and distribution.

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AN UNUSUAL CASE OF HYDATIDIFORM MOLE

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THIS is a rare type of benign penetrating hydatidiform mole with spontaneous rupture of the uterus at the site of penetration into the uterine wall. It is of particular interest because the uterus was not enlarged out of proportion to the period of amenorrhea, as frequently seen in hydatid mole.

This case, like another seen recently with hydatid mole, was first admitted to the medical service because of a supposed cardiac decompensation associated with a beriberi type of heart.

M. L., a 35-year-old colored female, was admitted to the Surgical Service of St. Philip Hospital April 27, 1939, complaining of irregular vaginal bleeding. Five months before entering the hospital she had a spontaneous abortion with free hemorrhage, and had continued to hemorrhage at irregular intervals.

Examination revealed a well-developed and poorly nourished colored female; temperature was 100° F.; pulse, 120; respirations, 50; and blood pressure, 120/80. She had a bronchopneumonia involving only the right lower lobe, and was dyspneic and orthopneic. Pelvic examination revealed a tender mass in the right fornix,

which extended down into the cul-de-sac and was fairly firm. The uterus was not definitely outlined, and the size of the mass was not noted. It was thought to be a tuboovarian abscess.

Laboratory studies revealed red blood cells 2,300,000, hemoglobin 28 per cent, white blood cells 5,900, polymorphonuclear leucocytes 76 per cent. Urinalysis was negative except for one-plus albumin and 20 to 30 pus cells per high power field.

The patient was transferred to the medical service for treatment of the pneumonia. On the medical service, dyspnea was thought to be due to cardiac decompensation with a beriberi type of heart. Blood chemistry studies revealed a moderate nitrogen retention, with nonprotein-nitrogen 45 mg., and a low total protein of 5.4 Gm. She was digitalized and put on restricted fluids and a low caloric, high protein, high vitamin diet. She was transfused once while she was

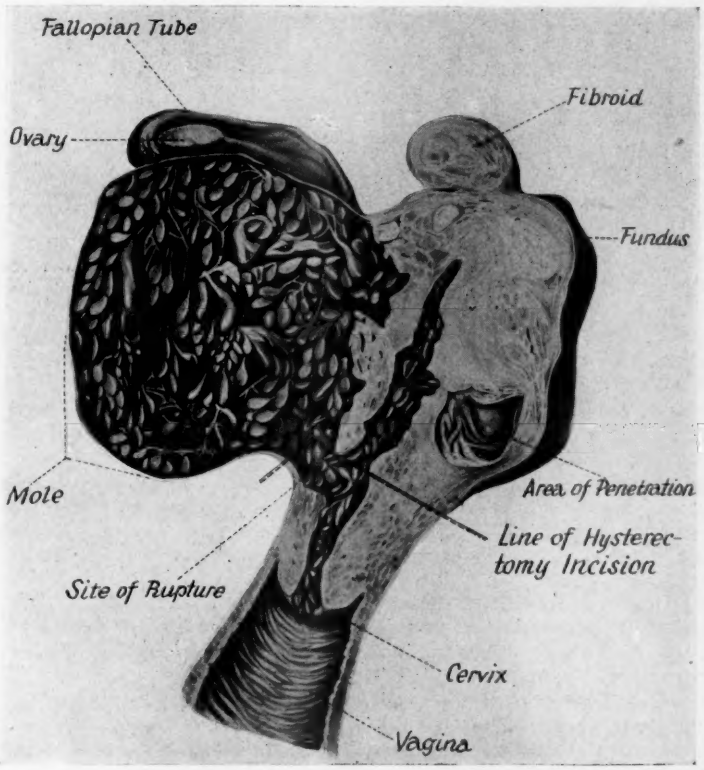

Fig. 1.—Drawing of reconstructed specimen.

on the medical service, receiving 500 c.c. of blood by citrate method, and showed a remarkable amount of improvement. She signed a release and left the hospital against advice, May 17, 1939. Her last blood examination showed red blood cells 1,800,000, and hemoglobin 34 per cent.

This patient was next seen on July 10, 1939, when she was admitted to the Obstetrical Service of St. Philip Hospital with a diagnosis of ruptured ectopic pregnancy. At this admission, a history was obtained that she fell on her abdomen about three weeks prior to admission, and had complained of moderately severe pain and weakness since that time. Her family doctor had repeatedly advised hospitalization, but she refused to take his advice.

Examination on admission to the obstetric ward revealed a well-developed, but poorly nourished, colored female, obviously in shock. She was very apprehensive, cold and clammy, and we were unable to obtain her pulse or blood pressure. She

had not been in shock when seen in the emergency room, and examination prior to her admission to the obstetric ward had apparently precipitated the shock. She was given ¼ gr. of morphine sulphate by hypodermic and 5 per cent glucose in normal saline, intravenously. Her blood pressure was then found to be 90 over 60, and her pulse was very rapid and weak. The heart rate and rhythm were regular; no murmurs were heard. Lungs were entirely clear. The abdomen was distended, very tense, and extremely tender throughout. A mass was outlined, extending out of the pelvis, to the level of the umbilicus in the midline. Pelvic examination revealed the entire right fornix bulging with a doughy mass which was extremely tender. This mass extended a little to the left of the midline, but the left fornix seemed normal. The cervix could not be made out, either on palpation or speculum examination. The mass in the right fornix seemed continuous with the mass in the lower abdomen. There was no blood or hydatid tissue in the vagina.

Laboratory studies revealed red cells 3,600,000, hemoglobin 58 per cent, white cells 18,250, polymorphonuclear leucocytes 77 per cent, and lymphocytes 23 per cent. A catheterized specimen of urine showed albumin 2-plus and 15 to 20 pus cells per high power field. The blood count was repeated at 2:30 P.M., two hours after the first count. It showed red blood cells 2,600,000, hemoglobin 28 per cent, and white blood cells 15,100. The urine was positive for acetone.

A donor was obtained, and the patient taken to the operating room for an exploratory laparotomy at 4:00 P.M. She was given oxygen, nitrous oxide, and ether for anesthesia, and the abdomen was opened through a right paramedian incision. Upon opening the peritoneum, a large amount of dark blood escaped under some pressure. The peritoneal cavity was found to contain both fresh and old blood clots, a total of probably 1,500 c.c. The uterus extended up to the level of the umbilicus. There were several small fibroids in the fundus and the anterior surface of the uterus. The fibroids varied in size from that of a marble to a walnut. A rupture 5 to 6 cm. in diameter, and more or less circular, was found on the posterior surface of the uterus. The uterus was lifted from the abdominal cavity, and a large amount of hydatidiform mole escaped from both the uterine and the abdominal cavities. There were several areas in the uterus which were apparently infiltrated with the same diseased process, which had almost ruptured. As much of the mole and blood as possible were removed from the abdominal cavity. The patient was bleeding freely at the site of the rupture, and a supravaginal hysterectomy was done. It was found that the cervical stump, uterine wall, broad ligament on the right, and possibly the ovary on the right were all infiltrated with the hydatid mole. The cervical stump was necrotic and friable. It was closed and peritonized.

The patient was transfused during the operation, receiving 550 c.c. of blood by citrate method. Her condition was very poor, and she was hardly breathing when returned to the ward. We were unable to obtain her pulse or blood pressure during most of the operation.

Upon returning to the ward, nasal oxygen was started, at the rate of 3 liters per minute, and increased to 6 or 7 liters per minute. She was transfused again four hours after operation, receiving 550 c.c. of blood by citrate method. Her blood pressure came up very slowly to systolic 120 and diastolic 80, and remained at this level for about six hours. Later, the blood pressure dropped to systolic 50 and diastolic 40, and remained at this level even after active treatment for shock. Six hours after operation her temperature was 103.6° F., and remained at that level. She died at 10:30 A.M., April 28, about eighteen hours postoperative.

Pathologic Report.—The reconstruction of the surgical and autopsy specimen showed a large mass of hydatiform mole, measuring approximately 9 cm. in diameter, situated in the right broad ligament and pelvic tissues. The mass was apparently in direct continuity with the lumen of the uterus through an opening in the right lateral wall of the cervix, approximately at the level of the amputation. The pelvic mass of hydatiform mole was well encapsulated and did not penetrate into the tube, ovary, or ureter. It was composed of irregular grapelike vesicles which varied extremely in size. Necrosis and hemorrhage were seen close to the hilus of the right ovary and near the site of amputation of the uterus.

A frontal section through the midportion of the uterus revealed that the latter was collapsed, but still showed hydatiform mole in its lumen which at various

points penetrated into the thick wall of the uterus, disclosing itself in form of smaller and larger cysts filled with thin mucoid material. At several points these cysts appeared underneath the serosa of the uterus.

Other gross findings were not pertinent. In view, however, of the disturbances of cardiac function, it must be mentioned that grossly and microscopically the heart was free from pathologic changes. Vacuolic disorder of myocardial fibers could not be demonstrated.

It should be mentioned that both ovaries were free from lutein cysts. However, the right ovary was adherent to the tumor mass and hemorrhage, necrosis, and a silk ligature were found at this point. A corpus luteum cyst previously present may have been destroyed and become unrecognizable. We can, therefore, not be absolutely sure that no corpus luteum cyst was present.

Sections through various portions of the hydatiform mole, outside and inside the wall of the uterus and through the endometrium, revealed the typical picture of a benign hydatiform mole characterized by large villi, the stroma of which was almost entirely free from vessels, edematous, with evidence of mucoid degeneration. In the center of many of the villi was found complete liquefaction necrosis of the connective tissue stroma. Most of the villi were covered by syncytial elements only, but occasionally both Langerhans' and syncytial elements were found. The Langerhans' cells, though scarce, were equal in size, cuboidal in shape with normally structured nucleus. The syncytial elements were those found in normal mature placental tissue with dense dark-stained nuclei, frequently forming buds, but there was no evidence of regressive changes, nor undue proliferation, nor independent growth of the chorionic-epithelial elements. The villi were seen within the wall of the uterus, but everywhere within preformed spaces lined by endothelial cells. These spaces were taken to be venous sinuses. It is of interest that the tissue immediately surrounding the sinuses revealed regressive changes resulting in almost complete necrosis of the connective tissue and the adjacent muscle bundles. This necrosis lacked inflammatory reaction, but was taken to be ante mortem, because it was found nowhere except in the immediate vicinity of such sinuses which were filled with chorionic villi.

COMMENT

The case is classified as one of the so-called penetrating hydatiform moles, which is sometimes referred to as "destructive hydatiform mole." Though limited penetration of the uterine wall by hydatiform mole is commonly found, massive growth in extrauterine tissues is apparently very rare.

Mathieu in his last collective review mentions 10 cases of uterine rupture due to penetrating hydatiform mole. It is difficult, however, to estimate the number of reported cases, because some of them have been misinterpreted as chorion epitheliomas. However, if the morphologic criteria laid down for the recognition of malignancy in general and for chorion epitheliomas in particular, are taken into consideration, our case offers exceptionally little difficulties in classifying it as a strictly benign growth.

The first and foremost histologic criterion of malignancy, namely, the independent growth of chorionic-epithelial elements is absent in our case. With few exceptions where groups of epithelial elements adhere to the inner lining of the uterine sinuses, the growth is strictly confined to the surface of the villi. Detached growth on the surface of blood clots is not encountered. The chorionic-epithelial elements do not infiltrate the stroma of chorionic villi. They show no autonomic proliferation exceeding the normal ramification of villi.

There is furthermore no definite anaplasia recognizable. It is, of course, not easy to apply our usual concept of the morphologic appearance of anaplastic cells to chorionic-epithelial elements. In this particular type of cells our criteria are not reliable if anaplasia is taken to be an indication of malignancy. We can, however, state that the chorionic epithelial cells in our case do not vary more in shape, size and staining effect than those seen in normal placentas. Mitotic figures are absent. Furthermore, the stroma of the villi does not actively participate in the growth, but merely reveals regressive changes.

Metastases have not occurred, the cell emboli in lung capillaries being regarded as normal.

In our histologic description, we mention a necrosis of the connective tissue surrounding the intravenously penetrating villi. This could be interpreted as the effect of a destructive character of the mole. However, every normal placenta is just as destructive. It produces fibrinoid necrosis known as zone of Nitabuch and even in the depth of the uterine wall coagulation necrosis can be observed about the villi which penetrate into the marginal veins or deeper into the veins of the muscular wall. The necrosis of uterine tissue in our case is not fibrinoid in character, but mere coagulation of the connective tissue matrix associated with loss of nuclei. This, however, is essentially identical with changes seen under normal conditions.

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SPONTANEOUS PERIRENAL HEMATOMA AS A POST-PARTUM COMPLICATION

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SPONTANEOUS perirenal hematoma has been previously described as a relatively uncommon entity. Conroy[1] reported 34 cases of aneurysm of the renal artery with hematoma, and additions were made to the literature by Drs. Meyer and Singer in 1927.[2]

We wish to report a case which followed a pregnancy. Hypertension, tuberculous or syphilitic infections, mycotic emboli, and blood dyscrasias played no role in the etiology. Trauma, however, is a questionable factor. A mass was observed after delivery, but it was only after a fall that this became more apparent with symptoms. The following case is reported because of its relative infrequency, and particularly because of its association as a post-partum complication:

I. W., colored female, aged 24 years, was admitted to the Cook County Hospital on Sept. 8, 1938, with a history of (1) pain in the abdomen for eighteen days, (2) mass in the right upper quadrant for seventeen days, (3) anorexia for one week, and (4) fever and sweats for four days.

The patient was delivered of a premature eight-month infant on Aug. 19, 1938, after an uneventful ante-partum course. Three days after delivery she noted a swelling in the right upper quadrant. Later that day she noted that the swelling became painful. This was considered of little significance, and she was discharged from the hospital on Aug. 27, 1938, although the mass was still present.

Four days after her dismissal, she tripped over a dog and fell. Soon after this incident she noted pain in the right shoulder, and the right upper quadrant pain, of which she had previously complained, became more severe. Four days prior to her readmission she began having chills and sweats. During the preceding two days she vomited at least twice daily.

Her menstrual history was normal, and the last period occurred Jan. 15, 1938. Her first pregnancy was a female infant delivered at eight months; second, a male at seven months, died at birth; third, a male at 8 months, living and well.

On physical examination her blood pressure was 100/80; temperature, 100.6° F.; and pulse, 110. She had a slight icteric tinge to her skin. Head, mouth, nose, throat, neck, lungs, and heart were all normal.

The abdomen was asymmetrically distended with a visible mass below the right anterior costal region and flank, which was about 10 cm. in diameter and very tender. The muscles overlying were quite tense. There was also marked tenderness in the right flank. The liver edge could be felt moving with respirations. Peristalsis was heard in the lower abdomen and was slightly obstructive in character.

On pelvic examination, the cervix was soft, and fundus soft and movable. Motion caused pain in the upper abdomen. The adnexa were negative, except

that pressure on the right side caused pain in the right flank. Pressure on the abdominal mass did not move the cervix.

The blood showed 2,350,000 erythrocytes, 50 per cent hemoglobin, 10,500 leucocytes, and the differential showed 74 per cent polymorphonuclears, 24 per cent lymphocytes, and 2 per cent monocytes. The blood Wassermann was negative.

The impression was: (1) liver abscess with hepatitis, (2) subhepatic abscess, and (3) high lying ovarian cyst with hemorrhage. Hydronephrosis and an ecchynococcus cyst were ruled out.

Conservative treatment, with bed rest, morphine, intravenous dextrose and saline, and blood transfusions, was instituted.

A flat plate of the abdomen revealed a soft tissue mass in the painful area and a high diaphragm with restricted movements. The bleeding time was 4 minutes 50 seconds.

She was cystoscoped but no pathology was noted. Ureteral catheters passed readily. Because of the mass, retrograde pyelograms were made. These revealed a normal right kidney pelvis, except for its position which was to the left of the midline at the level of the fourth lumbar vertebra. No deformity was noted on the left side.

A diagnosis of a retroperitoneal cyst was made and on Sept. 17, 1938, an exploratory operation was done by Dr. R. W. McNealy through a right paramedian incision. Here a large perirenal hemorrhagic cyst was found lying in the retroperitoneal space in the region of the upper pole of the right kidney. A diagnostic aspiration of 10 c.c. of hemorrhagic fluid was made. Iodoform gauze was packed between the cyst wall and the parietal peritoneum, so as to marsupialize the anterior wall of the mass.

On Sept. 24, 1938, she was re-operated upon and 2,500 to 3,000 c.c. of old blood and serum were removed from the cyst. Near the base, organized clots were obtained and after their removal bright red blood appeared. The cavity was then packed with two ten-yard uterine gauze rolls.

During the following week, the patient's course was very septic with chills, fever, and jaundice. On the eleventh postoperative day her course leveled off to normal.

After rehabilitation she went to surgery on Oct. 11, 1938, for a third time. On this occasion she was operated upon through a right lumbar incision. A large cystic mass originating from the upper medial pole of the right kidney or adrenal was found. The contents were foul smelling and suggestive of protein digested tissue. The cystic mass, right kidney, and adrenal were removed, and the wound closed, with the insertion of two Penrose drains.

On the first postoperative day her fluid intake was 3,550 c.c. and the urinary output 700 c.c. On the second postoperative day, the intake was 3,850 c.c. and the output 750 c.c. Her course from that time on was uneventful, and she was discharged from the hospital on Nov. 5, 1938.

Pathology.—Kidney 10 by 5 by 3.4 cm. Cortex stripped with ease and was pale tan gray. Attached to the anterior medial portion in the region of the pelvis was a stalk 6.5 by 2.5 by 0.5 cm., bearing a mass 25 by 15 by 5 cm. This had previously been opened.

Microscopic Findings.—Section of the cystic mass revealed dense edematous connective tissue wall which was very vascular and infiltrated by round cells. Lumina of the vessels were obliterated by blood clots, and there was marked proliferation of the intima. There was atrophic adrenal tissue encapsulated by proliferating scar tissue. The inner lining was of fibrin network with erythrocytes and a necrotic membrane with clouds of bacteria. The picture was that of an old organized hematoma or aneurysm.

On Oct. 13, 1939, one year later, she was delivered of a normal 8-pound male infant after an uneventful pregnancy.

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CARCINOMA OF THE FEMALE URETHRA

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SEVERAL reviews of the literature on carcinoma of the female urethra have been made in recent years. Counseller and Paterson,[1] in 1933, found a total of 124 cases and added 12 of their own. Menville[2] added 10 cases, bringing the total in 1935 to 149. Sparks and Parsons[3] reported a case in 1937 and tabulated the literature, making a total of 168.

Every attempt must be made to differentiate primary urethral carcinoma from secondary carcinoma arising in the labia majora or minora, vestibule, Bartholin's gland, clitoris, or vagina. Within the urethra the usual lesions which are to be differentiated are prolapse of the urethral mucosa, caruncle, fibroma, and sarcoma.

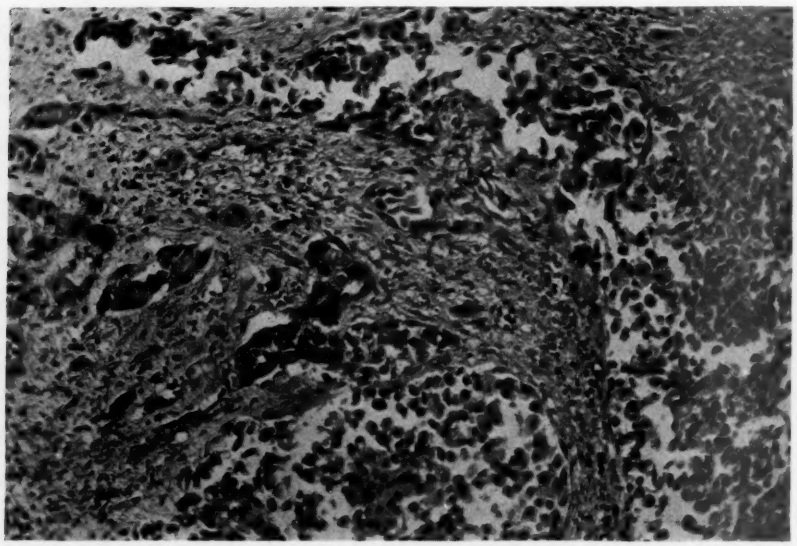

Fig. 1.—Squamous cell carcinoma invading the thin-walled cavernous spaces in the wall of the urethra. ×175.

A housewife, 57 years of age, entered the Grant Hospital of Chicago on June 6, 1938. She complained of genital bleeding and pelvic pain. A small palpable red mass had been present at the urethral orifice for three weeks. The menopause occurred eight years before. She had been married for eight years and had no children. An examination revealed a small, elevated, red ulcerated mass, involving the left lip of the meatus. Vaginal examination showed fixation of the entire urethra. A hard mass could be felt, and this gradually narrowed and disappeared at the bladder neck. The cervix uteri was not involved. No inguinal adenopathy was noted.

A suprapubic cystotomy was performed on June 10, 1938. The region of the bladder neck appeared indurated by tumor tissue. She left the hospital on June 29, 1938, and returned for roentgen ray treatments during July, August, and September. She was readmitted to the hospital on Oct. 7, 1938. At this time she

complained of vaginal bleeding and blockage of the indwelling catheter. The red blood count was 3,200,000 cells per c.mm. and the white blood count was 10,700 cells per c.mm. The nonprotein nitrogen was 91 mg. and the uric acid 8 mg. per 100 c.c. of blood. She died on Oct. 12, 1938.

At autopsy many blood clots could be expressed from the bladder through the cystotomy opening. The urinary meatus admitted a small probe. The entire length of the urethra was invaded by tumor tissue, the greatest thickness being near the meatus. The greatest thickness of the wall was 30 mm. on the left side and 12 mm. on the right side. The labia majora and minora were atrophic. The anterior wall of the vagina, trigone of the bladder, and anterior wall of the cervix were infiltrated by tumor tissue. A wooden applicator was inserted easily into each urethral orifice. The ureters were dilated on both sides. At the ureteropelvic junction, they measured 22 mm. in diameter. The pelvis and calices of the left kidney were moderately dilated. Both lungs showed extensive metastatic tumor nodules, measuring up to 2½ cm. in diameter.

Microscopic sections taken through the thickened urethra showed infiltrations of squamous cell carcinoma, many of the tumor cells being within the wide thin-walled venous channels. Slight hornification of the tumor cells was found in some areas. The metastases in the lung had a similar structure but without any traces of hornification.

SUMMARY

The infiltrating type of squamous cell carcinoma of the female urethra, if not recognized very early in the course of the disease, offers a very poor prognosis. Metastases can readily occur by way of the venous channels in the wall of the urethra.

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PROLAPSE OF A FALLOPIAN TUBE FOLLOWING VAGINAL HYSTERECTOMY

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BOWER, Pearce, and Conway, in the December, 1940, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, report a case of prolapse of Fallopian tubes with vaginal bleeding following vaginal hysterectomy. A similar incident occurred in one of our cases of vaginal hysterectomy, although the patient had no symptoms.

This patient, a 40-year-old married housewife, was referred to the hospital Jan. 23, 1936, for treatment of a badly eroded and hypertrophied cervix. Her only complaint was that of a gnawing pain in the left lower quadrant, especially noticeable during the previous two months. There were no associated urinary, gastrointestinal or menstrual complaints.

The systemic history was entirely negative. Catamenia began at 13 years of age, occurred regularly every four weeks, lasting from four to five days, except that in the last few months there had been some slight irregularity. The last menstrual period was Jan. 3, 1936. At no time had the patient experienced metrorrhagia, menorrhagia, or dysmenorrhea. She had been married nineteen years, having had six normal deliveries. The oldest child was eighteen years and the youngest, two years of age.

The physical examination revealed a rather thin white female, in no apparent acute distress. The patient was rather pale but presented no gross abnormalities. The secondary sex characteristics were well developed. The somatic examination was negative except for a few equivocal signs in the upper chest. Blood pressure

was 120 systolic and 80 diastolic. The breasts were moderate in size; no masses could be found. Abdominal examination revealed no masses, no herniations, and no points of tenderness. The abdominal musculature was rather poor. The liver, both kidneys, and spleen could not be felt.

Upon examination of the pelvis, a markedly relaxed outlet was found, with a fairly large cystocele and a moderate rectocele. The cervix, which was badly eroded, lacerated, and hypertrophied, protruded almost to the outlet. The uterus was in second-degree retroversion, soft, irregular, but normal in size for a multipara. Both adnexal regions were negative.

X-ray examination of the chest showed a slight tuberculous fibroid infiltration of apices of both lungs, with thickening of the pleura at the right base.

Diagnosis.—Cystocele; rectocele; first-degree prolapse of uterus; chronic endocervicitis with erosion, laceration, and hypertrophy.

Operation.—On March 7, 1936, a vaginal hysterectomy was done under gas ether anesthesia. A large gauze pack was used as a drain in the posterior cul-de-sac.

The course in the hospital was febrile. The gauze pack was removed on the fourth day following operation, but the patient had a temperature elevation rising to 102° F. throughout the first two weeks of the postoperative course. At one time a questionable mass was felt in the cul-de-sac, but this gradually subsided, as did the temperature elevation. The patient was discharged as cured on the twenty-fourth postoperative day.

On April 20, 1936, the patient returned for her first postoperative examination. Upon examination of the vaginal vault, an elongated granulating mass was seen protruding from its apex. The patient had no complaints, no vaginal bleeding, and no pain. A moderate amount of vaginal discharge was present, however. The primary result of the operation was good. The mass was avulsed and the base cauterized.

Microscopic examination of the tissue received revealed it to be a Fallopian tube.

IMPERFORATE HYMEN BEFORE THE MENARCHE WITH MUCOCOLPOS AND MUCOMETRIUM*

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IMPERFORATE HYMEN with hematocolpos is not rare. In 1939, Tompkins[1] reviewed 113 cases in the literature and added 5 more. Imperforate hymen before the menarche associated with an accumulation of mucus in the vagina and uterus probably has not been previously reported, and in view of its uniqueness this case is here recorded.

The patient was a 12-year-old twin Jewish girl who was admitted to the West Baltimore General Hospital, April 30, 1939. The patient had experienced mild right lower quadrant and midabdominal discomfort but had never had any pain. Bowel movements had been regular and there had been no emesis. During a routine examination, a mass was found in the lower abdomen. The child's mother had died from Hodgkin's disease. The child had never menstruated.

The patient was a well-developed and well-nourished girl. She was cheerful, intelligent, and cooperative. There was a symmetrical protrusion of the lower abdomen from the umbilicus downward. On palpation, a soft mass was felt, extending from the pelvis to the umbilicus. The mass was symmetrical and a questionable nodule was felt just to the right of the umbilicus. Rectal examination showed that the mass was smooth walled and in the midline. The pubic hair was well developed. Between the labia there was a pink, white spherical protrusion; and this was more prominent when the patient strained. The leucocyte count was 10,000 with 80

*This case is from the practice of Dr. S. H. Barranco.

per cent polymorphonuclear cells. The urinalysis and blood Wassermann were negative. Flat roentgenogram of the abdomen revealed a large mass extending up to the level of the third lumbar vertebra.

The patient was taken to the operating room on the third day after admission, and under evipal anesthesia an incision was made in the hymen. About 2 quarts of milky chylelike fluid escaped. The cervix was grasped with a tenaculum and a uterine sound was inserted 1½ inches into the uterus. A uterine pack was inserted loosely into the vagina. The vaginal pack was removed the following day and the patient was discharged.

The patient was seen by Dr. Barranco thirteen days after discharge, and at that time, vaginal examination revealed a slight mucoid discharge and an edematous cervix. Two months later the cervix was normal and the discharge was less. Hot potassium permanganate douches were advised. The patient was an identical twin, and her sister was examined at the time of operation and found to have a perforate hymen. This sister began to menstruate July 24, 1939, and the patient began to menstruate Oct. 10, 1939 (about five months following operation). The child's menstrual periods have been regular and there has been no dysmenorrhea. When the patient was examined fifteen months after operation, an adequate hymenal opening was found to be present, and at that time she weighed 105 pounds, having gained 15 pounds since operation.

A search of the literature reveals no similar case. We have compounded the terms mucocolpos and mucometrium which seem aptly to describe this condition. It is possible that a mucocolpos and mucometrium may exist before the menarche, and the onset of the menses may convert the mucoid fluid into a bloody one. This may be an explanation of some of the cases in which, with the history showing the patient to have been menstruating only one to two months, hymenectomy results in the evacuation of 500 to 1,000 c.c. of bloody fluid.*

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613 GREENLEAF BUILDING

TWIN TRANSVERSE PRESENTATION

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THE extreme rarity of twin transverse presentation makes this report of interest.

Mrs. P. C., an Italian woman, aged 32 years, was first seen in her sixth month of gestation on October 1. Her last menstrual period started on April 10, making the expected date, December 17. The general physical examination was essentially negative. Ten years ago, she was delivered at full term with low forceps, following an eighteen-hour labor, of a male child, weighing 10 pounds. The puerperium was uneventful. She became pregnant again, one year ago, which terminated in a complete spontaneous abortion at two months, with an uneventful recovery. Her pelvic measurements were ample in all diameters. She weighed 170 pounds. Abdominal examination at this time showed a uterus one-third of the way above the umbilicus and palpation was inconclusive. Pregnancy continued uneventfully up to the seventh month, when she developed a right-sided pyelitis, which was cleared up completely under Mandelic acid and ammonium chloride therapy. At the eighth month the uterus measured 39 cm. from the top of the symphysis, and twins were diagnosed. She started labor on December 21 which was eleven days past the calculated time. She was admitted to the Israel Zion Hospital the same date at twelve o'clock noon with contractions at seven- to ten-minute intervals, lasting thirty seconds. Labor had started six hours previously with the spontaneous rupture of the membranes. Rectal examination revealed an empty pelvis and the cervix could not

*See abstract at bottom of page 67 of this issue.—Editors.

be palpated. On abdominal palpation, the lowermost fetus was diagnosed as a right transverse, but the upper fetus could not be definitely outlined. Two fetal hearts of unequal rate were heard, being 140 and 160, respectively. At 3 P.M. an x-ray was taken, which revealed the lower fetus lying with the head in the right flank and the upper fetus also transverse, with its head under the spleen. At 4 P.M. she was taken to the operating room for a vaginal examination. The contractions, at this time, were every six minutes and of rather poor quality. On vaginal examination, the spinal column of the fetus was found directly across the cervix, which was two fingers dilated. the membranes being ruptured. It was felt that since the chances of her reaching full cervical dilatation spontaneously, in view of the presentation with ruptured membranes, were small, interference was indicated. A

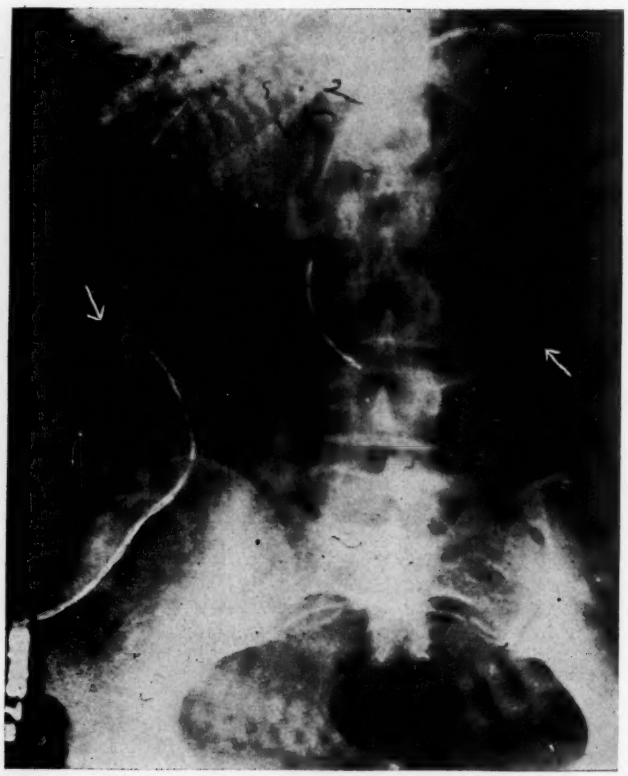

Fig. 1.—X-ray showing the lower fetus to be in a right transverse and the upper one to be in a left transverse position. The outlines of the heads has been accentuated.

foot was not brought down, as it was felt that there might be difficulty in bringing the lowermost body into a vertical position, due to the position of the upper fetus and also the danger of a prolapsed cord. Consequently, a No. 5 Voorhee's bag was inserted without any difficulty, and the patient was returned to the labor room. Three hours later, the contractions had increased in frequency to every four minutes and the bag, on rectal examination, was almost halfway through the cervix, which was a little over three fingers' dilated. No weight was used on the bag. At 9 A.M., the following morning, sixteen hours after the bag was inserted, it was expelled spontaneously, and she was immediately taken to the delivery room. The cervix was found fully dilated and the presenting part was still the middorsal spine of the fetus. The body was slightly rotated on its long axis, so that the feet could be more easily reached, and the version was slowly completed, followed by the extraction of

a living 5 pound 6 ounce male baby. An interval of ten minutes permitted the uterus to regain its tone, when the second bag of waters was ruptured. This fetus was found to lie with its lower right ribs towards the cervix, the head being in the left upper flank. The feet were brought down through the cervix and version and extraction resulted in a living 5 pound 4 ounce female child. No episiotomy was necessary as the pelvic floor was markedly relaxed. The placentas were expressed with a modified Credé method ten minutes later. There were two placentas separated by a narrow membranous cleft with separate amnions and chorions. The puerperium was uneventful, and she left the hospital in ten days with both babies.

DOUBLE PRIMARY OVARIAN MALIGNANCY

Granulosa Cell Tumor of the Ovary Following Radium Therapy for Cervical Carcinoma With Papillary Cystadenoma of the Same Ovary

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MULTIPLE malignancies are no longer considered a clinical rarity. It has been estimated by Warren and Gates[1] that 1.84 per cent of patients harboring malignant neoplasms have more than one primary malignant lesion. These tumors are usually found in the same organ or in organs of the same system or symmetrical systems, but may occur in different systems. Whereas multiple malignancies of the skin, large intestine, or stomach are observed relatively frequently, only a few cases of more than one malignant growth in the same ovary have been recorded. Major[2] in an extensive review of the literature in 1918 was able to find only three examples: one reported by Rahl-Ruckhardt,[3] a case of carcinoma and sarcoma of the ovary; Lippmann's,[4] a case of carcinoma sarcomatodes of the ovary; and Rothacker's[5] case of carcinoma and sarcoma of the ovary. In 1934, Bugher[6] cited one instance of multiple ovarian malignancy, an adenocarcinoma and a leiomyosarcoma of the ovary. Primarily because so few of these cases have been reported, the following case is presented.

REPORT OF A CASE

Mrs. W. F., aged 71 years, was admitted to Touro Infirmary, July 20, 1940, because of a greatly enlarged abdomen, weakness, and a loss of five pounds in weight. She did not complain at any time of uterine bleeding.

Twelve years before, on Sept. 25, 1928, she was seen for the first time, complaining of external vaginal pruritus of four months' duration and of a loss of 25 pounds in weight during the preceding three months. She had had five normal deliveries and one miscarriage. The menopause had occurred at the age of 51 years. Examination revealed a profuse pus discharge from the cervix. A diagnosis of chronic purulent discharge from the cavity of the uterus was made. Dilatation and curettage on Oct. 24, 1928, disclosed early squamous cell carcinoma of the cervix (Fig. 1). The patient was given 50 mg. of radium for twenty-four hours and 100 mg. for twenty-four hours or a total dosage of 3,600 mg. hr. She has been seen intermittently since that time. In 1936, a notation was made that the lesion had completely healed and that the uterus and adnexa were normal. In July, 1938, and again in August, 1939, pelvic examination showed the adnexa and cervix to be normal, the canal patulous, and the uterus small and in an anteverted position.

Pelvic examination on her last visit, July 18, 1940, revealed a normal cervix, no bloody discharge on probing the cervical canal and a greatly enlarged abdomen.

Fig. 1.—Section of biopsy, showing early squamous cell carcinoma of the cervix.

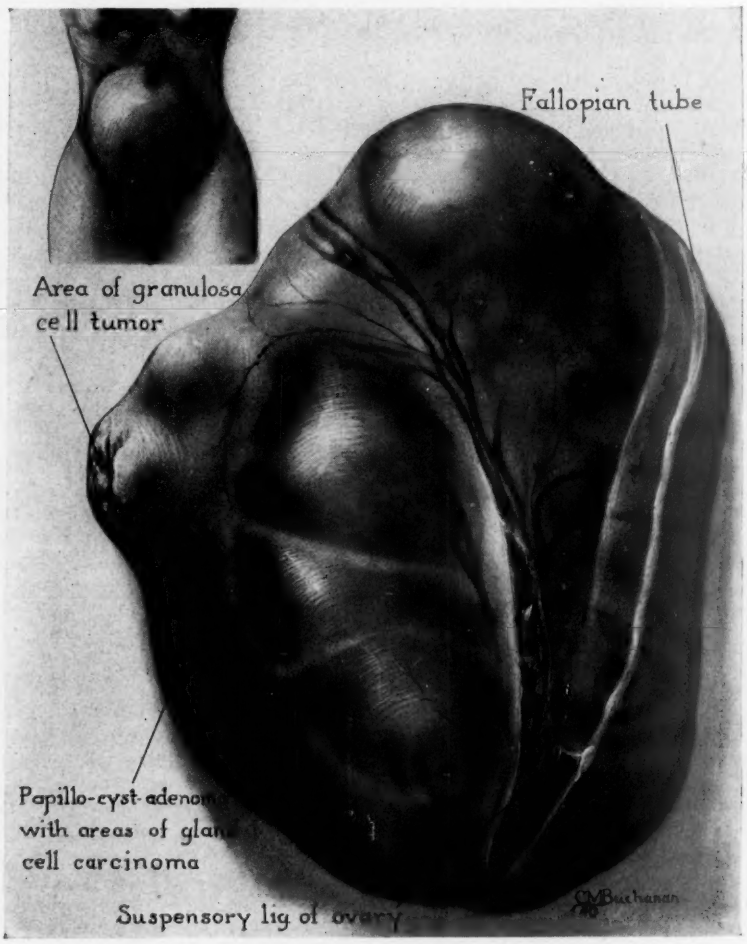

Fig. 2.—Encapsulated cystic tumor before sectioning.

Fluid waves were definitely present. Whether this was free fluid in the abdomen or an encapsulated mass was not determined at the time of examination. The chest was normal.

A diagnosis of malignancy of the ovary was made. Upon opening the abdomen, a large, multilocular cyst of the right ovary was encountered (Fig. 2). Exploration showed that the cyst had not ruptured and that there was no free fluid in the peritoneal cavity. The entire cyst was easily delivered from the abdominal cavity and removed intact. The tumor was well encapsulated and measured 22 cm. by 16 cm. by 11 cm. There were no cystic changes in the left ovary, but it was larger than would be expected for a woman of that age. Both ovaries and tubes were removed. The uterus was not removed because of the patient's age, because she had had previous radiation to the cervix and because the mass was well encapsulated.

The pathologist reported two distinct malignancies in the right ovary, a granulosa cell tumor and a papillary cyst-adenoma (Figs. 1 and 3). On microscopic examination no abnormal changes of the left ovary were noted.

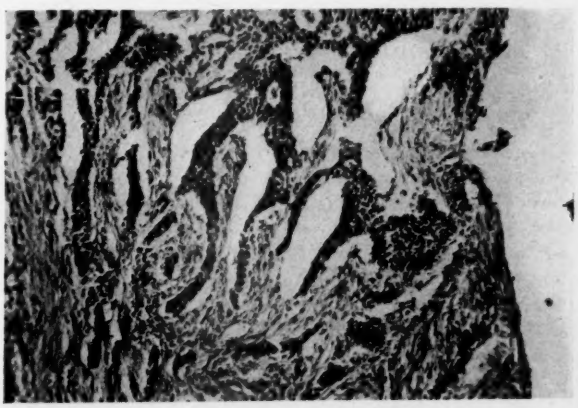

Fig. 3.—Section of right ovary, showing granulosa cell tumor invading ovarian stroma.

The patient's postoperative course was uneventful and she was discharged in good condition.

This case is of additional interest, because it represents a granulosa cell tumor of the ovary following irradiation therapy. Since the original description of a typical granulosa cell tumor of the ovary by von Kahlden[7] in 1895, a number of reports have appeared in the literature, so that now approximately three or four hundred cases have been recorded. Difficulty in collecting the reported cases has been encountered because of the diverse terminology employed before 1914, when von Werdt[8] suggested its current appellation, "granulosa cell tumor of the ovary." Attempts to clarify this confusion and to correlate the mass of clinical and histologic information were made by Te Linde[9] in 1930, Bland and Goldstein[10] in 1935, Pratt[11] in 1937, and Schulze[12] in 1939. Based on these series of collected cases, the clinical picture has been definitely established. However, the histogenesis remains a speculative problem, as attested by the numerous current etiologic theories.

We have had only one other patient with a malignancy following radiation therapy, a comparatively young woman with a cystadenoma of the ovary developing two years after intensive radiation for adenocarcinoma of the uterus. Whereas conclusive evidence remains to be offered, the possibility of irradiation as an inciting factor in the development of primary malignant neoplasms is too great to be disregarded. Because of the numerous factors involved and because the histogenesis of malignancies in general is still obscure, it is extremely difficult to establish such a premise.

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512 HIBERNIA BANK BUILDING

SEVERE MATERNAL TRAUMA IN EARLY PREGNANCY

CONGENITAL AMPUTATIONS IN THE INFANT AT TERM

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THE special interest of the present case lies in the occurrence of major trauma at about the close of the first trimester of pregnancy, and the delivery at term of an infant presenting multiple congenital amputations. A causal relationship between the maternal injury and the fetal defects cannot be established, but since the possibility is not absolutely excluded, the potential medicolegal aspects of this and similar cases are deserving of note.

Mrs. E. L. D., white, aged 29 years, was found in an unconscious state on a highway Jan. 6, 1940. She was still unconscious when brought by the police to the accident room at Charity Hospital. The patient exhibited an extreme degree of shock, blood pressure being 50/20. Fractures, multiple lacerations, contusions, and abrasions were present, and there was a partial avulsion of the scalp. A catheterized specimen revealed gross hematuria. The patient responded to shock treatment, the blood pressure rising to 100-120/50-70. She was given a double dose of mixed serum.

Upon regaining consciousness the patient explained that she had been walking alone on the highway. Though she could recall nothing of the accident, the circumstances point to her having been struck by an automobile. She was three months pregnant; the last menstrual period began about October 5. Her only previous pregnancy was normal, with delivery at full term about two years before.

X-rays were made, with the following findings:

1. Fracture of the right acromial process.

2. Fractures of the left pelvis at the junction of the ascending pubic ramus and the ischium and at the junction of the descending ramus and ischium.

3. Fracture of the sacrum, with no displacement.

4. Compound comminuted fractures of the lower halves of the right tibia and fibula, with overriding.

5. Fracture of the right parietal (from which the patient complained of persistent headache and diplopia).

Subsequent urinalyses showed no blood. A second double dose of mixed serum was given on January 7.

Appropriate fracture treatment was instituted. Osteomyelitis developed in the right leg about ten days after admission, in treatment of which a cast was applied and changed from time to time. She ran a low grade fever for three weeks. Quickening was first noted on February 15.

On April 14 the obstetric department was asked to see the patient. Neither before nor after this date was there any difficulty incident to pregnancy. There was no vaginal bleeding, and all the findings in obstetric examination were entirely normal. X-ray of the pelvis showed slight callus about the fractures, but there was no evidence of pelvic obstruction.

On May 4 the patient was discharged. She returned later for change of cast, and with approach of the date of expected delivery entered the obstetrical ward on July 8. The blood pressure was 120/80; pulse, 80; temperature, 98.4° F. A cast was still present on the right leg, which emitted a foul odor. The pelvic measurements were normal, the presentation was vertex R.O.P., and the fetal heart sounds were 140 in the R.L.Q. There was apparently no disproportion. A final x-ray of the pelvis showed no evidence of obstruction or bone displacement.

Labor began July 10. After a normal course for fifteen hours and 50 minutes a male child, weighing 6½ pounds, was spontaneously delivered. The child cried immediately at birth. The puerperium was uneventful and the mother was discharged eight days later. The infant was held in the hospital, where it has remained until the present time (January, 1941), for observation and treatment.

The infant presented multiple congenital amputations as characterized below, but otherwise there were no externally evident abnormalities. There were no abnormalities evident in the mother nor, according to her statement, in other members of the family.

1. The most conspicuous defects involved the right arm (Fig. 1). There was a deep cleft completely encircling the upper arm slightly above its middle (Figs. 1 and 2). The musculature of the lower arm and hand was atrophic (or hypotrophic?). The transverse dimensions of the lower arm and hand were smaller than on the left side, and there was a pronounced wrist drop (Figs. 1 to 3). All bones of the right arm and hand were less robustly formed than those of the left. The lower arm and hand were pallid and cold.

2. The left hand (Fig. 4) showed a completed amputation of the middle and terminal segments of the index finger and amputation of the terminal segment of the ring finger. There were several encircling and irregularly disposed clefts on the middle finger. Depending freely from the end of the index, there was a thin catgut-like strand, and there were several similar threads uniting the index and middle fingers.

3. On the right foot the distal segments of the first three digits were amputated, and their stumps were syndactylous.

A plastic operation was performed on the right arm with the aim of relieving compression at the level of the annular cleft. This was followed by improved circulation in the lower arm and hand, but the wrist drop has persisted. Except for a pneumonia, the infant has been in good health, and is now (January, 1941) about to be discharged.

The infant conforms to the typical picture of congenital amputations (Streeter[1]) with respect to the occurrence of multiple amputations and furrows, though it is unusual in presenting involvement at a level above the elbow. Portions of some digits are actually amputated, while the annular furrows of the right arm and of the middle finger of the left hand represent the same principle of affection, differently localized and expressed. The history of fetal amputations has been traced by Streeter[1] and the mechanism has been further discussed by Cummins[2] and Keith.[3] In Streeter's earliest specimen, of fourteen weeks' menstrual age, the process is already well advanced. When there is actual amputation, it is brought about by necrosis and sloughing, with occasional remains persisting in the form of strands, such as are observed in the left hand of the present case. The characteristic annular furrows are considered to result from local deficiency in the growth capacity of the tissues, of less severe grade than that leading to sloughing. Not uncommonly, as in the right foot of this case, there is coexistent amputation of digits and syndactylia of their remaining stumps. Coleman,[4] and others have raised the query as to whether there may be a causal relationship between these concurrent abnormalities. Our own conclusion is that the syndactylia is secondary to amputation,

the digits becoming joined by the reparative processes which follow amputation, in a manner similar to that in which secondary syndactylia may occur after severe burns if precautions are neglected.

It is now clear[1] that congenital amputations are not produced by any of the frequently suggested extrinsic mechanical agencies, such as ligature by amniotic bands or by the umbilical cord. The process operates intrinsically. While lack of vital

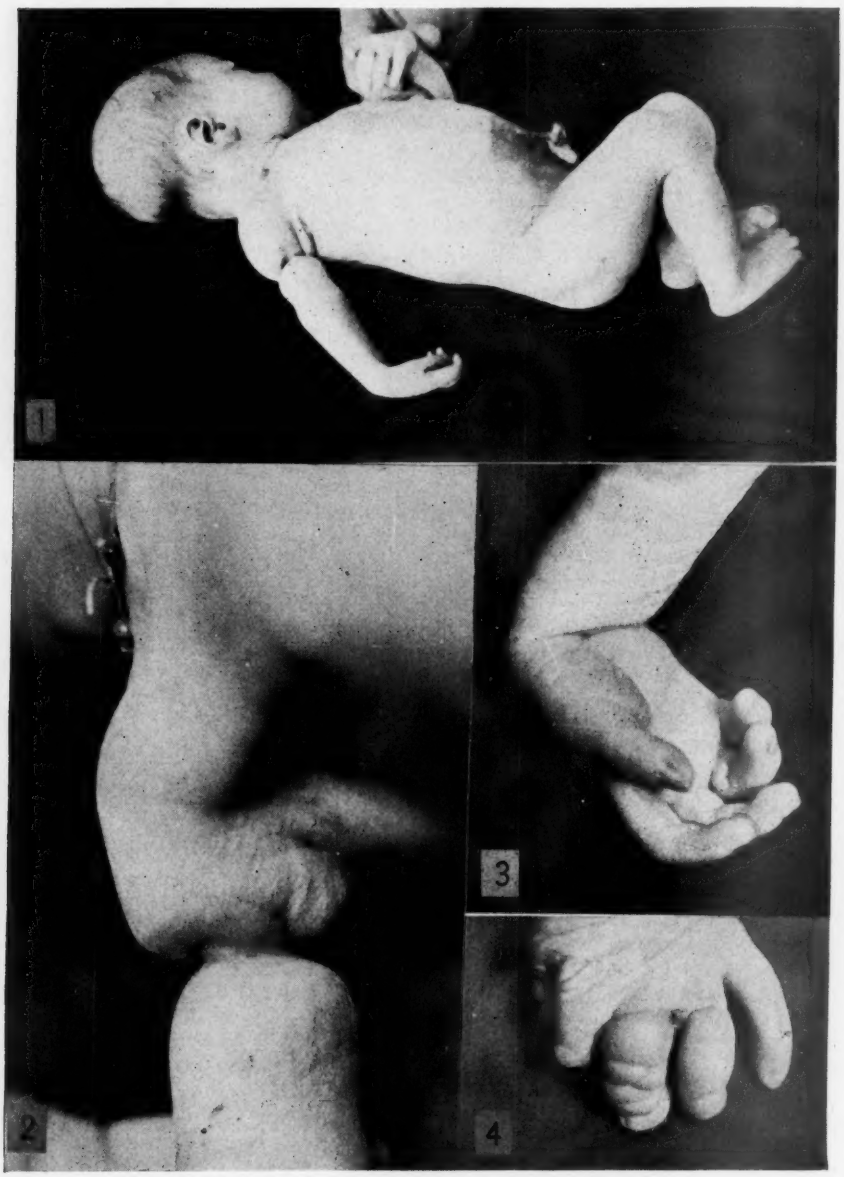

Fig. 1.—The infant at about one week.
Fig. 2.—The deep annular cleft of the right upper arm.
Fig. 3.—Right hand. Note wrist drop.
Fig. 4.—Left hand. Note amputation of index and furrows encircling the middle finger.

capacity of the tissues is demonstrated in the observed pathology of fetal amputations, a fully satisfactory explanation of its etiology is not yet available. From observations upon what is evidently the same condition in animals it appears that amputative processes arise primarily as a result of germinal defectiveness. Bagg and Little,[5] and Bagg[6] have produced in the descendants of x-rayed mice a large frequency of congenital defects, including clubfoot, polydactylism, and loss of distal portions of extremities. The x-ray exposure so alters the reproductive cells that embryos which they produce are thus defective. In rats without experimental treatment (Wooley and Cole[7]), the tail, toes, or rarely an entire foot may be involved in amputations, occurring usually between ten and twenty days after birth. This process in the rat has a germinal basis, and a probably recessive heredity. The deficiency may be regarded as due to a "susceptibility factor," for which the animal will suffer if other influences make it manifest. Again in the rat, a mild amputative tendency evident as slight annular constrictions is reported by McElroy and Goss,[8] arising in animals maintained on diets deficient in vitamin B_6; its appearance in only 10 per cent of the animals restricted to the same depletion diet is suggestive of a susceptibility factor.

From consideration of other reported instances of congenital amputations in human subjects* and of the parallel conditions observed in mice and rats, we conclude that the amputations in the present case are to be explained as the result of incapacity which was inherent in the developing embryo. But since actual manifestation of that incapacity might have been dependent upon the coexistence of other influences, the possible roles of known incidents of the prenatal history should be examined. The maternal injury in early pregnancy might be suggested as a possible source of developmental disadvantage. If it were a factor, the injury presumably would have operated mechanically, by disadjustment of the fetal-maternal circulatory relationships. There is the further possibility of vitiation of the fetal environment by toxic substances and fever incident to osteomyelitis. The brief x-ray exposures to which the fetus was subjected in making plates of the pelvis may be definitely ruled out as a causative agency. Neither of the two suggested possible factors can be absolutely excluded, though it would be difficult to substantiate their influence. On the other hand, there are two indications against etiologic significance of the maternal injury and its consequences. The more cogent is the conclusion of Streeter,[1] with which Keith[3] as well as the present authors agree, that the onset of amputative pathology is at a considerably earlier period than that of the maternal accident in this case. Second, congenital amputations occur in infants delivered by women having no history of trauma or infection, showing that such circumstances are not requisite for production of the defect.

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PREGNANCY COMPLICATED BY SEVERE GASTRIC HEMORRHAGE

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THE following case is being reported because of the rare occurrence of severe gastric hemorrhage occurring in a pregnant woman at term. Only two reports could be found in the literature on similar types of cases, and no mention of the subject could be found in any of the standard textbooks on obstetrics.

Sturrock,[1] in 1913, reported a case of gastric hemorrhage occurring at the time of delivery, but this case was in no way comparable to the one we are reporting. Subsequent studies were not done and no adequate explanation was given for its cause.

Preiss,[2] in 1907, reported the case of a woman who had a similar accident in her second and third pregnancies. Her first pregnancy was entirely normal. The second pregnancy, fifteen months later, and the third, three years after the second, were complicated by the occurrence of sudden severe gastrointestinal hemorrhages evidenced by vomiting of blood, passage of bloody stools, and shock. In both pregnancies, the bleeding occurred about two weeks before the expected date of confinement and was not associated with any previous gastrointestinal symptoms. In both instances, the onset of labor and delivery were spontaneous within twenty-four hours after the bleeding. The birth of normal, deadborn, male infants was the result in both pregnancies; the fetal hearts were lost during labor without any apparent cause. The puerperiums were normal in both pregnancies, and in the second pregnancy no special diet was given. The author discusses the possible causes of the bleeding and comes to the conclusion that it was due to a ruptured gastric varix produced by the mechanical stimulation of solid food.

Contrary to our experience, both Sturrock and Preiss make the statement that gastrointestinal hemorrhage during pregnancy is not an uncommon complication. In going over the records of the New York Hospital and the Berwind Maternity Clinic, no such complication occurred during labor in 27,942 deliveries. There was, however, one case of moderately severe hematemesis in a five months pregnant woman, who improved on bed rest and diet and went to term without further complications.

Our patient was a 31-year-old gravida ii, para i, who was admitted to the obstetrical service on Feb. 6, 1940, approximately one week before her expected date of confinement, because of vomiting of blood and passage of tarry stools for twenty-four hours. The first pregnancy had been uncomplicated and resulted in the spontaneous term delivery of a normal female infant, 3,220 gm., three years prior to the present pregnancy. The patient stated that during the latter months of her pregnancy she had vague attacks of indigestion, which she described as "heartburn," and that these often occurred during the night, following the ingestion of food before retiring. However, this symptom had been present during her first pregnancy and was similar to the complaints of a large percentage of pregnant women. For several days prior to admission she had had occasional dizzy spells and was easily fatigued. The pregnancy had otherwise been uncomplicated. The Wassermann test was negative. The weight gain was 20 pounds (from 114 to 134 pounds), and the blood pressure ranged petween 110 and 120 systolic over 70 to 80 diastolic. The urine on all occasions was free from albumin and sugar.

There had been no previous hematemesis or tarry stools. She gave a history of having had some gastrointestinal complaints in 1935. A gastrointestinal series, done at that time, showed a ptosis of the stomach and colon.

On admission at 4:00 P.M., the patient was rather pale but in good condition. The pulse was rapid but of good quality. The examination of the chest was essentially negative, the heart was not enlarged, rhythm regular, and blood pressure 125/85. She complained of nausea on palpation of the abdomen.

The red blood count was 3,020,000; hemoglobin 72 per cent Sahli. The urine showed no albumin or sugar, and the microscopic examination was negative.

At 6:15 P.M. she vomited 700 c.c. of partially clotted blood and complained of faintness and dizziness. The blood pressure fell to 96/50; pulse was 130 and of fair quality. Rectal examination revealed tarry stool on the examining finger. She was given 0.015 gm. of morphine sulphate every four hours by hypodermic injections with nothing by mouth. In addition to this, she was given a transfusion of 400 c.c. of citrated blood. Ice bags were applied to the upper abdomen. At 8:00 P.M. she vomited 300 c.c. more of older-appearing blood clots, but there was no appreciable change in her condition at this time.

The following morning the patient seemed more comfortable; the pulse was of good quality but was still rapid, 130 per minute; blood pressure 94/60; the hemoglobin was 62 per cent. No additional vomiting occurred. She was given another transfusion of 350 c.c. of citrated blood.

The fetal heart was not heard after 6 A.M., and fetal movements were not felt after this time. Labor started spontaneously at 9:00 A.M. The membranes ruptured at 9:05 A.M. The contractions at this time were mild, coming every seven to ten minutes apart. At 12 NOON the uterus was noted to be tetanically contracted but not tender; only the lower uterine segment relaxed between pains. At this time we thought that we were dealing with a premature separation of the placenta. The cervix at this time was effaced and 2 to 3 cm. dilated, with the head at the spines in an L. O. A. position.

Labor progressed rapidly and at 2 P.M. the patient was delivered by low forceps under light gas oxygen anesthesia. The baby was a deadborn, not macerated, male infant, weighing 2,530 gm. The placenta separated three minutes later and was expressed from the vagina by Schultze's mechanism. Gross and microscopic examination of the placenta revealed no evidence of premature separation or any other abnormality. The total blood loss was estimated at 50 c.c. Five hundred cubic centimeters of 5 per cent glucose were given following delivery, and the patient was returned to her bed in good condition.

At 9:00 P.M. another 500 c.c. of glucose were given. The patient was placed on a Sippy regime along with vitamin K by injection and vitamin C by mouth. Infusions of 500 c.c. of 5 per cent glucose were given on the first two post-partum days. There was no further hematemesis and the stools were negative for occult blood. Four cubic centimeters of iron ammonium citrate (50 per cent solution) were given three times a day.

On February 28, a gastrointestinal series revealed visceroptosis with no evidence of peptic ulcer or other pathology. Her diet was gradually increased, and she improved rapidly under conservative treatment and the administration of vitamins B and C. At the time of her discharge, four weeks following delivery, she was very much improved and feeling well. At this time her hemoglobin was 80 per cent and her red blood count 4,360,000.

Six weeks following discharge, the patient had no suggestive symptoms and had gained 5 pounds in weight. The blood pressure was 126/70, hemoglobin 96 per cent, and red blood count 4,700,000. Physical examination was essentially negative. Since that time, the patient has been perfectly well.

DISCUSSION

On admission to the hospital it was felt that the patient had either a bleeding peptic ulcer or a ruptured varix. In view of the negative gastrointestinal series, the patient, in all probability, had a severe gastritis with subsequent erosion of a blood vessel. Not infrequently do we see individuals who have a severe hemorrhage with subsequent x-ray examinations failing to reveal any defects. Hemorrhage is merely an incident and may bear little relation to the size, the site, or even the

presence of an ulcer or eroded area. Hematemesis may be associated with a variety of conditions, and it may be very difficult or even impossible to demonstrate the etiologic factor.

We are at a loss to explain any cause for the intrauterine death of the fetus and the tetanic state of the uterus during labor. Strangely enough, the case reported by Preiss produced the same result. We might postulate, tentatively, that severe gastrointestinal bleeding might affect the uterine circulation sufficiently to produce the syndrome characterized by death of the fetus and tetanic contraction of the uterus. Yet the same result is not associated with hemorrhage from placenta previa.

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WATERS CESAREAN SECTION IN A PATIENT WITH GAS BACILLUS AND MIXED INFECTION

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THE Waters section for infected patients may be an outstanding contribution to obstetric surgery. The original communication[1] establishes its anatomic superiority over similar operations and, with a series of 60 cases without maternal death, suggests technical safety. But its behavior in the clinical test of actual infection still is unproven: only 1 of Waters' 60 patients is recorded as infected, although 14 had preoperative fever. And we have found no other papers on the operation. Nowadays infections serious enough to offer it a stringent test are unusual.

CASE REPORT

A 32-year-old primipara (Clinic No. 14711) had dependent edema (Grade 2), albuminuria (Grade 4), evidences of severe pyelonephritis, and blood pressure of 155/82 with, incidentally, a history of systolic pressure over 200 for some weeks before. We saw her first after seventy-two hours of satisfactory labor pains, when, despite the absence of bony disproportion and with no history of cervical disease or operation, the cervix still was only one finger dilated. Several vaginal examinations and attempts at manual and instrumental dilatation had been made since rupture of the membranes, which had preceded by eight hours the onset of pains. There was a thin, foul vaginal discharge. The temperature was 100.2° F., the weak pulse 120 and the leucocyte count 20,500.

After four hours' rest by morphine, during which sulfanilamide and parenteral fluids were begun, a Waters section under spinal anesthesia and a transfusion were done. It was recorded that opening the uterus released "a stench like that of appendiceal peritonitis, not at operation but at autopsy." The baby died the next day, and post-mortem examination showed general sepsis of two or three days' estimated duration. The mother's convalescence was stormy, with uremia, serum sickness, metastatic infections, and septicemia. Despite a large subperitoneal abscess, evacuated by rectum on the thirteenth day, there was no evidence of peritonitis, and she was discharged relieved on the thirty-sixth day. The organisms recovered from the uterine cavity were hemolytic staphylococci and streptococci, various bacilli, and *Clostridium welchii.*

The chief postoperative treatments were double-time Elliott therapy, sulfanilamide, and, for the gas bacillus, roentgen therapy and antitoxin.

COMMENT

Here was a patient, already a doubtful risk from toxemia and pyelonephritis, with cervical dystocia and established virulent infection by the gas bacillus* and other organisms following a long dry labor. A Waters section was done. The child died but the mother lived.

The method of operation apparently kept walled-off from the peritoneal cavity, and within the range of chemo-, sero-, heat and roentgen therapy, a large subperitoneal abscess.

Waters' operation is extraperitoneal from start to finish and gives exposure that is really surgical. Its relative simplicity is no small argument for a technique which, fortunately, few of us often will need to use. The case reported here suggested two further simplifications:

Technically, the crux of the operation is the separation from the bladder of the deepest layer of perivesical fascia, the layer directly on the vesical veins. Along the midline, especially anteriorly at the urachus, this fascia is fused tightly to the bladder. Also, the guiding veins are fewer in the midline. Start the dissection, then, as in cystectomy: not right across the dome, but separately on each side of the midline, and continue separate dissections all the way down to the uterus itself. At this depth the midline fusion has ceased, and a finger can pass from side to side. On this finger as a guide, cut the tensed median line of fusion by sharp dissection.

Finally, we would suggest draining via the anterior vaginal vault rather than uphill through the incision.

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PURPURA HEMORRHAGICA COMPLICATING PREGNANCY

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PURPURA hemorrhagica is an uncommon complication of pregnancy, there being approximately 75 instances reported to date. Purpura may appear during pregnancy in its primary or idiopathic form[1] and also as a secondary or symptomatic manifestation of either latent toxemia[2] or drug allergy.[3] Multiparas are more often affected than primigravidas, and the dyscrasia tends to occur in the latter half of pregnancy.[1] It is, in any case, a serious complication, with a mortality of more than 55 per cent.[4]

The case history herein recorded is of unusual interest because the patient, having previously had a nephrectomy for carcinoma, underwent a subtotal thyroidectomy because of hyperthyroidism in the first trimester of pregnancy, developed purpura hemorrhagica during the second trimester, prematurely delivered previable triplets, suffered several severe post-partum hemorrhages, and recovered.

CASE REPORT

Mrs. E. S. (Mount Sinai Hospital No. A 18863), white, twenty-one years of age, was admitted to the hospital on March 13, 1940, because of threatened premature labor at six months of pregnancy in association with bleeding from the gums and epistaxis.

The patient first came under observation in 1935 when, at the age of sixteen, her left kidney was removed because of hematuria and the presence of a palpable tumor.

*For a discussion of the role of *Cl. welchii* in intra-partum infection, see Cosgrove and Barry.[2]

The latter proved to be a tubular adenocarcinoma. Following several courses of roentgen therapy to the operative site, the patient remained perfectly well until the initiation of pregnancy in the fall of 1939. Her last menstrual period had occurred on Sept. 7, 1939, and the patient required hospitalization on Dec. 7, 1939, because of hyperemesis gravidarum associated with severe tachycardia and marked weight loss. The basal metabolic rate was found to be plus 64 per cent. Medical treatment for hyperthyroidism was instituted and, on Dec. 29, 1939, with the basal metabolic rate reduced to plus 32 per cent, subtotal thyroidectomy was performed. The patient's convalescence was uneventful, the state of gestation remained undisturbed, and she was discharged from the hospital on Jan. 21, 1940, with a basal metabolic rate of plus 14 per cent. A few days later, on Jan. 24, 1940, the patient reported quickening. In the middle of February, she first observed several petechiae on both arms and, shortly thereafter, experienced bleeding from the gums and epistaxis. Hospitalization was occasioned two weeks later because of increased mucosal bleeding and the appearance of painful uterine contractions.

On admission to the hospital, the patient was afebrile, had a blood pressure of 122/76 and presented no signs of toxemia. There was moderate bleeding from the gums and from both sides of the nasal septum. The uterus, palpable to just above the navel, contracted vigorously at irregular intervals. Fetal motion was apparent, but fetal heart tones were not audible. On rectal examination, the cervix seemed to be uneffaced and undilated. Laboratory studies at this time revealed the presence of a hypochromic anemia, with the level of hemoglobin at 70 per cent (Sahli), and a platelet count of 140,000. Coagulation, bleeding, and clot retraction times, the prothrombin determination and a Wassermann reaction were all normal. The medical consultant suggested the diagnosis of "symptomatic purpura, possibly related to the recent hyperthyroidism." The daily treatment included the intramuscular injection of 2 mg. of progesterone and the intravenous administration of 100 mg. of cevitamic acid in 250 c.c. of matched whole blood. The uterine contractions abated and the patient seemed to improve.

At 4 A.M., March 18, 1940, five days after her admission, the patient was awakened from sleep by the initiation of premature labor which terminated six hours later with the spontaneous delivery of female triplets. Each of the first two infants was stillborn, macerated, measured 32 cm. in crown-heel length and weighed less than 700 Gm. The third baby, weighing 706 Gm. and measuring 33 cm. in crown-heel length, was feebly alive at birth but died three hours later. The placenta and membranes delivered spontaneously ten minutes after the birth of the last child. The patient suffered no laceration but bled profusely (more than 800 c.c.) from the uterus which failed to contract, despite the use of obstetric pituitrin, ergonovine, and a firm intrauterine pack of 5 yards of two-inch gauze. The patient continued to bleed through the packing, and the uterus was repacked after thirty minutes. She was given 1,000 c.c. of 10 per cent solution of glucose intravenously and, shortly thereafter, 500 c.c. of matched whole blood. Post-partum treatment included the oral administration of ergonovine, the hypodermic use of moccasin snake venom, and a daily blood transfusion. The epistaxis ceased and the bleeding from the gums diminished.

Forty-eight hours after her delivery, the patient began to bleed through the previously undisturbed uterine packing. The uterus was repacked with three-inch iodoform gauze and the same therapeutic regimen continued. The bleeding from the mucosal surfaces ceased and the uterine packing remained dry. The latter was removed after seventy-two hours, on the fifth post-partum day. No further hemorrhage occurred. The patient was febrile while the packing was in place but remained free from temperature after the seventh post-partum day. At the time of the patient's discharge from the hospital, on April 3, 1940, the fifteenth post-partum day, the uterus was well involuted, the hemoglobin value was 76 per cent (Sahli) and the platelet count was 200,000. The patient, maintaining her weight and menstruating normally, has remained well to date (January, 1941).

Pathologic Report.—The triple cord placenta, 18 cm. in diameter, was studded throughout with areas of focal hemorrhage which were especially prominent about

the umbilical veins. The post-mortem examination of the triplets revealed no gross abnormalities, but multiple areas of cerebral hemorrhage were noted in each by histologic examination.

SUMMARY

The history of a 21-year-old primigravida, salvaged from adenocarcinoma of the kidney, is presented because she survived hyperthyroidism and purpura hemorrhagica during pregnancy. The former responded to subtotal thyroidectomy; the latter resulted in premature labor and severe post-partum hemorrhage. Two of the previable triplets, prematurely delivered three months prior to term, were stillborn, and the third died several hours after birth.

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TREATMENT OF SYPHILIS IN PREGNANCY

A Comparison of Arsenicals

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IN SEPTEMBER, 1938, at the Colored Division of Grady Hospital, Atlanta, it was decided to compare the use of mapharsen, the hemialcoholate of parahydroxyphenylarsine oxide hydrochloride, with that of neoarsphenamine in the prevention of congenital syphilis.

The patients studied were all negroes. The only criteria used in the two series were that each prospective mother should have a positive Wassermann or Kahn test before treatment was started and that each patient studied should have received at least 10 treatments with either mapharsen or neoarsphenamine at weekly intervals during the course of her pregnancy. In the vast majority of the patients both Wassermann and Kahn tests were positive.

METHOD

We specified at least 10 treatments so that we could form a comparison of the value of the two drugs. Our experience has taught us that this number of treatments will, as a rule, prevent congenital syphilis. To give only 10 treatments with one of the arsenicals, however, is not the routine of our clinic. We give weekly injections of one of the arsenicals from the time the patient presents herself until the termination of pregnancy unless some contraindication arises. Consequently, many of the patients included in both the mapharsen and neoarsphenamine series received as many as 27 weekly treatments of one drug or the other.

The conditions under which the two drugs were given were the same, with one exception. All patients attended the same morning clinic and all received the same antenatal instructions regarding diet, care of the bowels, etc. Distilled water was used as the diluent in both series. The one exception was that 25 c.c. of distilled water was used to dilute the dose of neoarsphenamine and only 10 c.c. was used with mapharsen.

The weekly dosage of neoarsphenamine was 0.45 Gm. In the mapharsen series there was some variation in the dosage. The first patients treated with mapharsen received 0.03 Gm. at each injection. Finding that the drug was well tolerated and believing this amount inadequate, we changed the dosage six weeks later to 0.04 Gm. Ten months later we again increased the dosage of mapharsen, and we are now giving 0.05 Gm. Since this study covers the period from Sept. 1, 1938, to March 1, 1940, the majority of the mapharsen patients received the 0.05 Gm. dose. None of the patients included in the study received all 10 treatments of mapharsen in the 0.03 Gm. dosage.

TABLE I. COMPARISON OF FETAL MORTALITY AND SEROLOGY IN MOTHER

	TOTAL NUMBER OF MOTHERS	FULL TERM ALIVE		PREMATURE ALIVE		BORN DEAD OR DIED		NEGATIVE LABOR SEROLOGY	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Mapharsen	155	125	80.64	24	15.48	8	3.88	65	41.93
Neoarsphenamine	116	101	87.07	10	8.62	6	4.31	45	38.79

RESULTS

One hundred and fifty-five patients treated with mapharsen and 116 patients treated with neoarsphenamine are included in this study (Table 1). In the mapharsen series, there were 80.64 per cent full-term live babies, 15.48 per cent premature alive, with 3.88 per cent born dead or dying in the hospital. In the neoarsphenamine series comparable figures are obtained: 87.07 per cent full-term live babies, 8.62 per cent premature alive and 4.31 per cent born dead or dying in the hospital. In the mapharsen series, 41.93 per cent and in the neoarsphenamine series 38.79 per cent showed negative blood tests.

There were two sets of twins in the mapharsen series and one set in the neoarsphenamine series.

TABLE II. COMPARATIVE FOLLOW-UP STUDIES OF LIVE BABIES

	TOTAL NUMBER OF LIVE BABIES	BABIES RECEIVING FOLLOW-UP EXAMINATIONS		TOTAL NUMBER PROVED SYPHILITIC	PER CENT TOTAL PROVED SYPHILITIC	PER CENT FOLLOW-UP PROVED SYPHILITIC
		NUMBER	PER CENT			
Mapharsen	147	84	57.14	6	4.08	7.14
Neoarsphenamine	110	64	58.18	5	5.54	7.81

Table II presents a comparison of the follow-up study on the live babies delivered in the two series. The follow-up study included a Wassermann or Kahn or both on all the babies reported upon, with a complete physical examination in the majority. Eighty-four babies were examined in the mapharsen series, or 57.14 per cent of the live babies in this series. This latter figure is comparable to the one obtained in the neoarsphenamine series, i.e., 64 reports, or 58.18 per cent. In the mapharsen series, 6 babies, or 4.08 per cent, were proved to be syphilitic; in the neoarsphenamine series, 5, or 4.54 per cent, of the babies were proved to be syphilitic. Figuring the percentage of babies with proved syphilis on the basis of the number of reports obtained, we again arrive at comparable figures: in the mapharsen series 7.14 per cent and in the neoarsphenamine series 7.81 per cent of the babies were syphilitic.

Table III is a detailed analysis of the babies that were born dead or that died in the hospital. All had x-ray studies of the long bones. All these x-ray films were read by one person. Only two of the dead babies had any of the signs of congenital syphilis. Both of these weighed less than 1,500 Gm.; both were in the

TABLE III. DETAILED STUDY OF DEAD BABIES

CASE	WEIGHT AT BIRTH GM.	DRUG*	X-RAY REPORT ON BONES	
1	540	Maph.	Positive	10 treatments, 3 of which were 0.03 Gm.
2	1,400	Maph.	Positive	10 treatments, 5 of which were 0.03 Gm.
3	1,100	Maph.	Negative	
4	1,240	Maph.	Negative	
5	2,310	Maph.	Negative	Intrauterine death 20 hr. after proved gross intra-partum infection.
6	1,810	Maph.	Negative	Respiration poor. Impression of atelectasis. Autopsy refused.
7	1,490	Maph.	Negative	Anatomic diagnosis: Prematurity, congenital atelectasis of lungs, acute dilation of the heart.
8	1,310	Maph.	Negative	
9	2,100	Neo.	Negative	Mother had cardiovascular disease. Blood pressure 230/140 during labor. Catheter and bag induction. Prolonged labor. Autopsy refused.
10	1,140	Neo.	Negative	
11	2,460	Neo.	Negative	Spontaneous delivery. Short labor. Clinical diagnosis cerebral hemorrhage. Autopsy refused.
12	2,185	Neo.	Negative	
13	2,630	Neo.	Negative	Intrauterine death probably due to short cord. Autopsy refused.
14	2,410	Neo.	Negative	Anatomic diagnosis: Tentorial tear with massive intracranial hemorrhage. Also congenital atelectasis of lungs.

*Maph., mapharsen; Neo., neoarsphenamine.

first group of patients that received only 0.03 Gm. of mapharsen per injection. In the first case, there were 5 doses of 0.03 Gm. and in the second, 3 doses. We believe that an inadequate amount of arsenic was used in these cases, and that they are no reflection on the drug.

There were no severe reactions, immediate or delayed, in either series. Local reactions caused by technical accidents were about the same in the two series. The only notable difference in the toxic reactions was that nausea following the administration of mapharsen did not seem to be as frequent or as severe as with neoarsphenamine.

SUMMARY AND CONCLUSIONS

1. Best results in the prevention of congenital syphilis are obtained by early and continued treatment with one of the arsenicals throughout the duration of pregnancy.

2. Mapharsen will prevent congenital syphilis as well as neoarsphenamine and in the patients so far studied is better tolerated.

511 DOCTORS BUILDING

SULFONAMIDE SUPPOSITORY IN THE TREATMENT OF ACUTE GONORRHEA IN WOMEN

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IT IS well known that ambulatory treatment of acute gonorrhea has always been attended by a large incidence of complications, including Bartholin abscess, chronic Skenitis, salpingitis, and endocervicitis. Nevertheless, economic considerations still demand ambulatory treatment in many patients, and this study was made on such a group.

The last two years have seen many publications describing the treatment of acute gonorrhea by the oral administration of sulfonamide. It is interesting to note that the urologist has been more enthusiastic about his clinical results than has the gynecologist. This may be due to the chemotherapeutic effect of the drug passing over the male urethra after being excreted by the kidney.

In this out-patient service, 25 cases of acute gonorrhea were observed and proved by history, laboratory, and pelvic examination. These patients were treated by the oral administration of sulfonamide, 80 gr. daily for the first three days, and 60 gr. thereafter for two weeks. Bi-weekly examinations of the blood and urethral and cervical smears were taken. In this group, treated as described, without any local therapy, one patient had a negative smear at the end of one week; 3 patients had negative smears at the end of two weeks. The other 21 patients had clinical and laboratory evidence of gonorrhea when the seventeen-day course of therapy was completed. Eighteen of the 25 cases could be followed for three months. During this period 3 of them developed a Bartholin's abscess, 4 developed evidence of salpingitis, 16 had a persistent endocervicitis, and 6 had a subacute Skenitis. It could not be concluded from the results in this series that sulfonamide administered orally, in the absence of other treatment, was a satisfactory means of treating gonorrhea in women.

Two young girls, aged 4 and 9, were seen with acute Neisserian vaginitis. They were treated with 40 and 30 gr. of sulfonamide, respectively, administered for a period of seventeen days. No laboratory or clinical change in the vaginitis could be seen at the end of the treatment.

After being disappointed by the oral administration of the drug, we observed another series of patients with acute gonorrhea, using the drug locally. Insufflation of the powder was first used but promptly discarded because the powder has a tendency to cake in the vaginal vault, and does not come into contact with the urethra and vaginal introitus. The sulfonamide then was incorporated in a boroglyceride base, using 20 gr. of sulfonamide and 10 gr. of lactose in the suppository. Twenty-five patients suffering from acute gonorrhea were treated by the insertion of one sulfonamide suppository high into the vaginal vault three times a day.

These patients were treated for seventeen days, smears from the urethra and cervix being taken biweekly. It was noted that the symptoms of dysuria and purulent leucorrhea disappeared in 12 of the patients on the third day. Smears from the urethra and cervix were negative in all 25 patients at the end of one week. It was possible to follow 21 of the 25 for a period of three months. Nineteen patients were symptom-free without evidence of urethritis, and there were no cases of bartholinitis. There was not a single case of salpingitis. One patient, at three months, had an acute gonorrhea which could be traced to an intercourse five days previously with a male suffering from a recently acquired urethral discharge. This patient stated that she had been symptom free up until the onset of this reinfection. One patient had a residual endocervicitis. The most remarkable feature of these 19 cases was the absence of any endocervical infection, this being confirmed by the absence of pus cells in the cervical smears.

Two cases of acute vaginitis in children were seen. Local treatment by insertion of sulfonamide suppository resulted in laboratory and clinical cure within the seventeen-day treatment period.

A careful review of the literature failed to show any report on blood levels of sulfonamide, following the introduction of the drug into the vagina. Twenty-five adult patients treated by the vaginal route were studied at the end of one week, during which time the adult patients had each received 420 gr. of sulfonamide, and the children had each received 280 gr. The blood levels varied from a trace to 4 mg. per 100 c.c. of blood. The higher concentrations were found in children with acute vaginitis. Obviously, the clinical result could not be attributed to the drug which was absorbed. It does demonstrate again that the vaginal mucosa is an absorptive organ, and therefore, care should be exercised in the introduction of new drugs.

CONCLUSIONS

1. Oral administration of sulfonamide for the treatment of acute gonorrhea in women has little if any value.
2. Sulfonamide locally in the form of boroglyceride suppository probably has real value in the prevention of complications and cure of infection.
3. Sulfonamide is absorbed from the vaginal mucosa in varying degrees, the degree of absorption being more apparent in patients with acute vaginitis.

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SIMPLIFIED SUCTION FOR OBTAINING ENDOMETRIAL BIOPSIES

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THE value of endometrial biopsy in gynecologic and endocrine diagnosis is obvious, even though Israel and Mazer[1] believe that the removal of small pieces of tissue is of no value, especially in suspected malignancy. Various types of instruments, however, have been devised for the removal of such specimens from the uterus with minimal danger and discomfort to the patient. These include a tiny curette (Hoffmann[2]), an endometrial punch (Lorinez and Davis[3]), and the more commonly used cannula with the closed end and the side opening, the biopsy curette (Klingler and Burch[4]; Novak[5]; Randall[6]). Modifications of the latter instrument have been made by Kurzrok, Wilson and Cassidy.[7] With the punch or biopsy curette, in order that the portion of the endometrium be removed and not lost in the uterine cavity, suction is applied. This pulls the tissue back into the hollow shaft of the instrument, and allows the operator to remove three or four sections without withdrawing the instrument from the uterus.

Suction may be applied either with a glass or metal syringe, equipped with a three-way stopcock *(8)*, or with an electric pump, similar to a breast pump, and connected to the curette by means of a suction bottle and rubber tubing *(3)*. Both of these methods possess disadvantages. The former requires the use of both hands in manipulating the syringe, gives an intermittent type of suction, and possesses an added hazard, in that the operator, forgetting to turn the stopcock before closing the syringe, forces both air and the tissue specimen back into the uterine cavity. The particular disadvantages of the latter method lie in its excessive bulk and unwieldiness, together with its inherent power to ruin the specimen by excessive amounts of suction.

Since the above methods are not satisfactory, the following simple means of applying either negative or positive pressure to the biopsy curette is recommended.

The apparatus consists essentially of a metal Luer nipple to fit the machined end of the curette, a length of thick-walled rubber tubing, and a DeVries aspirator bulb, the end of which is modified so that it can be held firmly between the lips and

teeth. These three pieces are combined into one unit and may be attached to the curette after it has been inserted into the uterus, but before the specimen has been scraped from the uterine wall. By gentle or forceful suction on the bulb, the pressure may be modified at will.

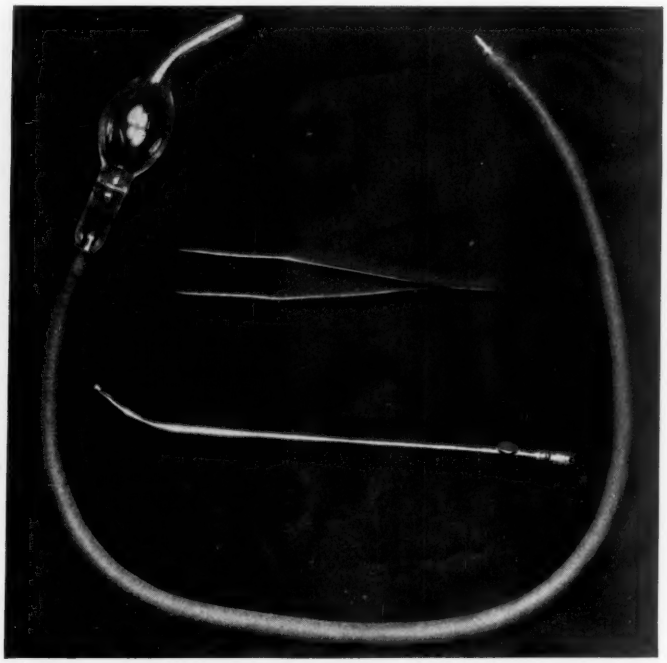

Fig. 1.

In this way, the hands are left completely free for the manipulation of the curette. Two, three, or four specimens may be removed, and easily sucked up into the shank of the instrument. Furthermore, after the curette has been removed from the uterus, the tissue may either be expelled by blowing through the tube, or may be picked out of the curette with a sterile forceps. Thus the curette may be kept sterile, so that if the necessity for removing further specimens arises, it may be reinserted into the uterus without danger of infection.

For office work, it is to be recommended that the entire outfit, including the curette, tubing, bulb, tissue forceps, and gauze be wrapped and autoclaved in a single unit.

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935 Park Avenue

Editorial

The Role of Iso-Immunization in Transfusion Accidents in Pregnancy and in Erythroblastosis Fetalis

IN THE course of studying transfusion accidents in pregnancy, observations were made which are of particular interest to the obstetrician and pediatrician.[1-4] These findings paved the way for an improved compatibility test which should considerably diminish the incidence of hemolytic transfusion reactions. Furthermore, the studies revealed data which served as a basis for a theory on the pathogenesis of erythroblastosis fetalis in its various manifestations.

Such transfusion reactions are not due to errors in blood grouping, but are attributable to the presence in the mother's blood of immune intragroup agglutinins. There is evidence that a newly discovered factor[5] in human red blood cells, Rh,* if present in the fetus and absent in the mother, can stimulate the mother to produce anti-Rh agglutinins. The Rh factor which is present in 86 per cent of individuals of the white race is inherited as a dominant property, much like the A and B factors of the four blood groups.[6]

It is probable that anti-Rh agglutinins are responsible for about 90 per cent of all intragroup transfusion accidents, after repeated transfusions or in pregnancy at the first transfusion. In short, a certain proportion of Rh negative individuals can produce anti-Rh agglutinins either by immunization with the Rh factor of the fetus or by repeated transfusions with Rh positive donors. This process is referred to as isoimmunization, since the individual producing the antibodies and the individual yielding the immunizing material are in the same species.

In many instances anti-Rh agglutinins react far better at 37° C. than at lower temperature. For this reason the term "warm agglutinin" was applied to them. In this respect they differ from the agglutinins of the grouping sera and other atypical agglutinins. It is, therefore, recommended that in the direct compatibility (cross-matching) the patient's serum and donor's cell suspension be incubated for thirty minutes at 37° C. and then centrifuged at low speed (500 r.p.m.) for one minute.

The modification, i.e., incubation at 37° C. is highly essential for the proper selection of a compatible donor, especially in obstetric and

*The sera of rabbits prepared by injection of rhesus (Rh) blood and the sera of some pregnant women, serve as reagents to detect this blood factor.

[1] *Levine and Stetson:* J. A. M. A. **113**: 126, 1939.

[2] *Levine and Katzin:* Proc. Soc. Exper. Biol. & Med. **45**: 343, 1940.

[3] *Levine, Katzin, and Burnham:* Proc. Soc. Exper. Biol. & Med. **45**: 346, 1940.

[4] *Levine, Katzin, and Burnham:* J. A. M. A. **116**: 825, 1941.

[5] *Landsteiner and Wiener:* Proc. Soc. Exper. Biol. & Med. **43**: 223, 1940.

[6] *Landsteiner and Wiener:* Personal communication.

gynecologic practice, since a readily available source of anti-Rh agglutinins for the selection of Rh negative donors is not yet obtainable. Even if an Rh negative donor of the same blood group is on hand, the compatibility test as indicated should not be omitted.

An analysis of the obstetric histories of the women who suffered from hemolytic transfusion reactions because of isoimmunization revealed a high incidence of spontaneous abortions and miscarriages, stillbirths, and neonatal deaths.[2] The clue to this relationship became evident when the bloods of a larger series of women giving such obstetric histories were studied.[4] It was found that these women in many instances showed a striking familial incidence of babies with erythroblastosis fetalis. In the great majority of cases, the bloods of these women were found to be negative for Rh while the bloods of their husbands and their affected infants contained this factor. In a certain proportion of the cases the mother's blood contained anti-Rh agglutinins of varying degrees of intensity.

These findings suggested that erythroblastosis fetalis is the result of (1) isoimmunization of the Rh negative mother by the Rh blood of the fetus and (2) the subsequent passage of mother's agglutinins through the placenta to act on the susceptible blood of the fetus.

Philip Levine, M.D.

Eschweiler, Paul Chadbourne: Dangers of the Indiscriminate Coverance of Parenterally Administered Glucose With Insulin, Surg., Gynec. & Obst. 71: 141, 1940.

A usual preoperative or postoperative procedure is to give an infusion of 500 c.c. of 10 per cent glucose "covered" by 25 units of insulin in cases of diabetes mellitus complicated by obstetrical or surgical conditions. Too frequently a hypoglycemic reaction results. A study has been made to determine whether all patients with diabetes mellitus can be expected to tolerate the same amount of insulin with an infusion of glucose. Intravenous glucose tolerance tests were given to 5 patients with diabetes mellitus of various stages of severity and to 1 normal patient. It was determined that insulin is not required to reduce the blood sugar values near to the fasting level after the intravenous administration of 500 c.c. of 10 per cent glucose, as the blood sugars of the patients with diabetes mellitus reached blood sugar levels approximating their usual fasting levels within one and one-half to two hours. It was demonstrated that the milder the case of diabetes the more nearly was approached the curve representing the nondiabetic patient. It may be concluded, therefore, that insulin should never be routinely administered to "cover" parenterally administered glucose in patients with diabetes mellitus. The diabetic status of the patients must be taken into consideration and thus dangerous hypoglycemic reactions may be avoided.

WILLIAM C. HENSKE.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology

Novak's *Gynecological and Obstetrical Pathology, With Clinical and Endocrine Relations*[1] for the first time assembles and documents the unusually large and long experience of the author in teaching these branches. His effort has been to produce a book which should neither err on the side of too great brevity and superficiality, nor on the other hand, fall into the class of encyclopedic exhaustiveness which would relegate it to a book of reference. This aim has been fulfilled only partially as it will have little appeal to gynecologic pathologists, except in the chapter devoted to the physiologically active ovarian tumors.

The author takes a considerable knowledge of general pathology for granted, wisely, so it appears to me, as unless this basis is already present, neither student nor practitioner would be in a position to evaluate specialistic knowledge. Throughout, the clinical side has been given due weight, with consequent direct applicability of the pathologic findings to clinical medicine. Although the hormonal basis of female genital disturbances is dealt with most briefly, they are described lucidly. This applies particularly to the phenomena of menstruation and the so-called functional diseases of the endometrium. There is an ample and beautifully reproduced collection of microphotographs with proper emphasis on the more common disturbances. A chapter by Dr. Louis M. Hellman on the diseases of the placenta, not including hydatidiform mole and chorionepithelioma, is incorporated. The illustrations of macroscopic conditions are mainly from well-known sources to which due credit has been given and are quite adequate in most instances.

This book will be found of great value to the advanced undergraduate student as well as to the practitioner in studying gynecologic pathology. It will likewise be of utmost use in the study of gynecologic pathology in medical schools where the pathologic material is limited. The short references at the end of each chapter will likewise prove of use in finding the later literature to the appropriate subjects.

R. T. Frank.

With the increasing application of the knowledge of the physiology of the ductless glands to practical problems in the treatment of endocrine disorders, a host of books and articles have been presented in this field. The latter has grown to enormous proportions so that considerable effort is required by the student and practitioner to keep abreast of the advances in the same. Among recent additions is the comprehensive monograph by Hamblen entitled *Endocrine Gynecology*,[2] which is addressed primarily to the practitioner. For that reason, it may be designated as timely and likewise authoritative, because its author has made many contributions to the literature based on personal observations and experiments on endocrinology as applied to gynecology. As stressed in the Foreword by Prof.

[1]**Gynecological and Obstetrical Pathology, With Clinical and Endocrine Relations.** By Emil Novak, Associate in Gynecology, Johns Hopkins Medical School, etc. 496 pages with 427 illustrations. W. B. Saunders Company, Philadelphia, 1940.

[2]**Endocrine Gynecology.** By E. C. Hamblen, B.S., M.D., F.A.C.S., Associate Professor of Obstetrics and Gynecology, Duke University School of Medicine, etc. With a foreword by J. B. Collip, M.D. Charles C Thomas, Springfield, Ill., and Baltimore, Md., 1940.

J. B. Collip, there is a wide divergence between laboratory animal experiments and their application to the human subject, and nowhere is this "species difference" more evident than in the field of sex physiology. It demands collaboration between the clinician and the laboratory which unfortunately is not given sufficient attention. In actual practice the alluring reports emanating from commercial sources often are accepted without restraint and account for failures that may discredit a most valuable remedy. Dr. Hamblen in his presentation is satisfactorily conservative and therefore his book may be commended. It presents the results of careful personal studies in addition to complete summaries of the work of others. An important item is the frank discussion of the various commercial preparations which have become so numerous in recent years that confusion as to their employment is to be expected. Perhaps this portion of the book should have followed rather than preceded the very full description of gynecic physiology and endocrinopathic gynecology. The book is attractively printed and very fully illustrated, although many of the photomicrographs appear inadequate as to size. The bibliographic references at the close of each chapter are ample evidence of the ground covered by the author's reading, as is the subject index. The book constitutes a very valuable addition to American textbook literature.

George W. Kosmak.

Mazer and Israel have written a large monograph on the *Diagnosis and Treatment of Menstrual Disorders and Sterility.*[3] According to them, it is designed as "a guide to the family physician"; to me it appeals as a rich and valuable storehouse of the world's literature covering these subjects, the result of meticulous scanning, careful selection, and correct application.

The symptomatology, the clinical investigations, the office procedures, the explanations of basic principles underlying the various hormonal and other tests are admirably and lucidly described. This praise likewise applies, almost unqualifiedly, to the four introductory chapters which deal largely with the physiologic features of the sex cycle, although I am unwilling to concede that "A late menarche is the signpost of an adolescent endocrine disturbance. . . ." "Attempts, therefore, should be made to correct endocrine deficiency in girls before irreparable damage to the lower genital tract ensues." This dictum requires many qualifications.

The authors, in my opinion, subdivide and catalogue symptoms, such as amenorrhea and uterine bleeding, into exact categories far more rigidly than our present knowledge warrants, and upon this most insecure basis employ and recommend therapeutic measures with an exactitude and selectivity which likewise are entirely unwarranted. The reader will find few conditions for which active therapy is not recommended and still fewer in which, according to the authors, he may not anticipate gratifying results.

The volume concludes with nine chapters dealing with all phases of sterility, including that of the male, habitual abortion, and mechanical and endocrine factors.

R. T. Frank.

This book, *Diseases Affecting the Vulva,*[4] by a well-known British dermatologist deals with dermatologic conditions of the external genitalia. While written ostensibly for the specialist in gynecology, it is so elemental in its approach that it would seem more suitable for the medical student. The first eighth of the volume describes the anatomy and embryology of the organs under discussion. While an attempt is made to present the various clinical conditions as pathologic entities,

[3] **Diagnosis and Treatment of Menstrual Disorders and Sterility.** By Charles Mazer, M.D., F.A.C.S., Assistant Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania, etc., and S. Leon Israel, M.D., F.A.C.S., Instructor in Gynecology and Obstetrics, School of Medicine, University of Pennsylvania. With 108 illustrations, 485 pages. Paul B. Hoeber, Inc., New York City, 1941.

[4] **Diseases Affecting the Vulva.** By Elizabeth Hunt, M.D., Ch.B. (Liverp.), Honorary Physician to the Skin Department, South London Hospital for Women, etc. With 36 illustrations and 18 plates in color. The C. V. Mosby Company, St. Louis, 1940.

this effort is not consistent. The photomicrographs leave much to be desired, many being poorly reproduced. There are eighteen gross color plates, which are well done. That these, however, have not been selected with reference to the relative importance of the various conditions is evidenced by the fact that eleven of the eighteen illustrate varieties of lichen planus. No effort is made to give any accurate data regarding either the incidence or prognosis of the diseases discussed. This is especially reprehensible in the chapter on neoplasms. Furthermore, such important methods of therapy as the use of chemotherapeutic agents in gonorrhea and of estrogenic substances in vulvovaginitis in children are given only cursory attention.

L. M. Hellman.

The second edition of Robson's *Recent Advances in Sex and Reproductive Physiology*[5] has appeared after an interval of six years. The advances in this comparatively short time have been huge and have necessitated much revision, and yet the author has succeeded in keeping the monograph within small compass (329 pages). The new chapter on standardization and determination of activity of the sex hormones is specially à propos and valuable. No clearer, more concise or juster presentation of the present state of this constantly advancing field of biology and medicine can be found.

R. T. Frank.

The third edition of Maguire's *The Anatomy of the Female Pelvis*[6] for the first time is illustrated by excellent and very simple line drawings, based on dissections of sixteen female pelves. This monograph is of value because it gives a simple and readable description of all the pelvic structures in the female, corresponding to all well-accepted anatomic details.

R. T. Frank.

Obstetrics, etc.

Six years ago, Dr. Stander revised the last edition of Prof. Williams' classic textbooks on obstetrics.[7] Advances in this branch of medicine have dictated a complete rewriting, with the result that little of the original text remains unaltered. Old chapters have been re-arranged and several new chapters added: "Diseases and Abnormalities of the New-Born," "Classification of Abnormal and Contracted Pelves," and "Sudden Death and Maternal Mortality." Numerous sections have been rewritten and brought up to date in accordance with developments recorded in obstetric literature. The author's own views are featured, based on the principles taught and practiced in his hospital and medical school affiliations and experiences.

We are dealing practically with a new work in this important branch of medicine which is a worthy successor to the outstanding earlier editions of a man who is generally regarded as one of the foremost American teachers of obstetrics. Professor Williams' textbook for many years occupied an important place in American medical literature. It is a classic which has retained through the labors of Dr. Stander in this Eighth Edition its accepted place as a guide to both student and practitioner.

George W. Kosmak.

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[5] **Recent Advances in Sex and Reproductive Physiology.** By J. M. Robson, Lecturer in Pharmacology, University of Edinburgh. With introduction by Professor F. A. E. Crew, Director of the Institute of Animal Genetics, Edinburgh. Second edition, 329 pages with 62 illustrations. Blakiston Company, Philadelphia, 1940.

[6] **The Anatomy of the Female Pelvis.** By F. A. Maguire, Honorary Lecturer in Anatomy; Honorary Gynaecological Surgeon, Royal Prince Alfred Hospital and Prince Henry Hospital in Sydney. Third edition, 162 pages, Illustrated. Angus and Robertson, Sydney, Australia, 1940.

[7] **Williams' Obstetrics.** A Textbook for the Use of Students and Practitioners. By Henricus J. Stander, M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Cornell University Medical College; Obstetrician and Gynecologist-in-Chief, New York Hospital and Director of the Lying-in Hospital, New York City. Eighth Edition. D. Appleton-Century Company, Inc., New York and London, 1941.

Dr. Greenhill offers an excellent manual in his *Obstetrics in General Practice.*[8] The book is intended primarily for the general practitioner; the text is clear and concise; and is well illustrated. There is an excellent outline of prenatal care and a discussion of minor ailments during pregnancy. As a matter of fact these two chapters deal with most conditions of which the average pregnant woman complains. Although Greenhill quotes frequently from recent literature, one can feel that many of the practical suggestions offered are those which have been found most useful in his hands.

In his discussion of toxemia of pregnancy, the author presents the new classification proposed by a Sub-Committee on Toxemia of the American Committee on Maternal Welfare. Each group and its major subdivisions are thoroughly explained, so that the differentiation of types of toxemias in the hands of the general practitioner should not be difficult. Although Greenhill has stressed the hormonal cause of eclampsia, according to White, in his consideration of diabetes, he does not make mention of this etiologic factor in the discussion of eclampsia itself. The mechanism of labor and operations occasionally necessary for delivery are well described and illustrated. In an excellent chapter on post-partum care he stresses the need for medical attention during the post-puerperal period. Illustrative tables suggest the dosage of the sulfanilamide compounds in sepsis. There is a short closing chapter on obstetric endocrinology.

This is an excellent book; well arranged; well illustrated; essentially practical; and may be highly recommended to those in general practice.

Philip F. Williams.

The fascinating story of twins and other multiple pregnancies has been presented for lay readers in *Multiple Human Births*[9] by Horatio Hackett Newman, and appears under the aegis of the American Association for the Advancement of Science. The author has made a special study of twins for over twenty-five years and has written a book which should be both interesting and educational not only for the layman but for those with a more scientific background. There are discussed the facts and fictions of twins, types and evaluations, with descriptions of typical and unusual experiences. Special attention is paid to the one-egg Dionne quintuplets. The author describes this remarkable group from a biologic standpoint, and tells many details of their development, education, and personalities. One can regret with the author that the study of the mental and personality differences of the quintuplets, which was carried on for several years, has ceased at the order of their guardians. The author does not regard the "quints" as shining examples of the wonderful effects that environment and training are supposed to produce. Why one-egg twins have an apparent mental telepathy and other similar qualities is explained. On the other hand there is a contrasting record of the life story of one-egg twins who have been reared apart.

This book will answer many questions the general public is fond of asking, will satisfy the amateur biologist, and will allay certain fears harbored by many twins and their parents.

Philip F. Williams.

Since the subject of birth control is as widely accepted today as any other prophylactic measure in medicine, it is well to have such a definite and practical manual as *Techniques of Conception Control*[10] available for physicians and those engaged in public health work. In this small but beautifully illustrated pamphlet, Dickinson and Morris have discussed practically all methods of contraception.

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[8] **Obstetrics in General Practice.** By J. P. Greenhill, M.D., Professor of Obstetrics and Gynecology, Loyola University Medical School, Chicago, etc. 448 pages, 112 illustrations. Year Book Publishers, Inc., Chicago, 1940.

[9] **Multiple Human Births.** By Horatio Hackett Newman, Ph.D., Sc.D., Professor of Zoology, University of Chicago. Illustrated, 214 pages. Doubleday, Doran & Co., New York, 1940.

[10] **Techniques of Conception Control.** By Robert Latou Dickinson, M.D., and Woodbridge Edwards Morris, M.D., General Medical Director, Birth Control Federation of America. 50 illustrations, 56 pages. The Williams & Wilkins Company, Baltimore, 1941.

The application of these various methods is clearly described and illustrated and should assist in the adequate instruction of married couples in the proper desire to space children. The authors regard the control of conception of equal importance in medicine with the control of infection, pain, and communicable diseases.

This type of presentation of the subject will do much to advance the control of conception to its proper place in the community.

Philip F. Williams.

Since contraception is becoming an integral part of every maternal health program such a report as this *Controlled Fertility: An Evaluation of Clinic Service*[11] by Regine K. Stix and Frank W. Notestein is important. The authors have attempted to show the effects of contraceptive practices on fertility, to evaluate the influence of the clinic services, and to consider the place of such a clinic as an agency of public health and welfare. The patients of the Birth Control Research Bureau in New York have been used in this group study. Some question arises as to whether or not this group was a conditioned one, as 96 per cent of them had practiced some form of contraception before they attended this clinic. A new statistical approach is made to the problem by using pregnancy rates instead of case failure ratios.

Some interesting statements are noted in regard to the difference in birth rates in three religious groups. Of the pregnancies occurring in these clinic patients, less than 70 per cent ended in live births, while more than 20 per cent were terminated by illegal abortion. The authors state that this is a very much higher proportion of pregnancy wastage than in any other group for which there are data concerning pregnancy terminations. The authors regard the birth control movement as a too single-minded limitation of fertility, and are in agreement that the decline in national fertility has been primarily due to increased use and effectiveness of contraceptives. They state there should be more emphasis on the positive aspects of birth control and more consideration of the high value of the new life.

Philip F. Williams.

For two centuries Sweden had a rapid population growth. Then suddenly in a land of democracy and social advances a sharp decline occurred in the birth rate. This was so steep as to cause considerable concern and when brought to the attention of the population a Commission on Population in Sweden was appointed to study the situation, a situation which is not at all peculiar to any one country. This *Report on the Sex Question,*[12] which is largely due to the efforts of Professor Gunnar Myrdal and Dr. Andreen-Svedberg, presents a review of the situation since 1935. The question has been studied from sex, social, political, and hygienic standpoints.

More than half of the book is devoted to the consideration of the ethical principles and evaluation of contraception. Venereal diseases and sex education are also discussed. There can be little doubt that the spread of contraception has had a marked influence in the family life of that country but the authors feel that child care and family protection are also essential facts in promoting the fertility which will be necessary to keep the population of Sweden at even a stationary level.

Philip F. Williams.

The second edition of this book *Modern Marriage*[13] by Paul Popenoe has taken cognizance of the advances of sociology and education for marriage during the

[11]**Controlled Fertility: An Evaluation of Clinic Service.** By Regine K. Stix, M.D., Research Associate, Milbank Memorial Fund, and Frank W. Notestein, Ph.D., Lecturer in School of Public Affairs, Princeton University. The Williams & Wilkins Company, Baltimore, 1940.

[12]**Report on the Sex Question.** By the Swedish Population Commission. Translated and edited by Virginia Clay Hamilton, M.D. Published for the National Committee on Maternal Health, Inc. By Williams & Wilkins Company, Baltimore, 1940.

[13]**Modern Marriage.** By Paul Popenoe, General Director, American Institute of Family Relations, Los Angeles, Calif., etc. Second edition, 299 pages. The Macmillan Co., New York, 1940.

past fifteen years. The expansion of this line of thought has made it necessary for an entire re-writing of the book which may properly be taken to represent the ideas of the American Institute of Family Relations. The book is primarily addressed to men. In a highly practical, common-sense manner many points of the various phases of marriage are discussed. To the physician, sociologist, or minister, who has contacts including young people seeking information either for premarital education or solution of the problems of marriage, this book is a source of information of the highest quality. It is so written that it may be handed safely to any man, or indeed to any woman, who is contemplating marriage.

Philip F. Williams.

Dr. Corner talks to girls about sex in this small book *Attaining Womanhood*[14] in clear, understandable and easy language. He has described without any sensationalism the reproductive cycle in animals and human beings, and the development of the girl's body before maturity, explaining her physical and mental changes as she passes through the adolescent period. He then describes and discusses sex life in a frank and simple manner and closes the book with a short discussion of the venereal diseases. In this day when so many abnormal aspects of sex life are depicted or suggested by screen and press, it might be well for this book to be read by girls even a little younger than the group for which Dr. Corner intended it.

Philip F. Williams.

Fetus; Newborn; Child

The scattered and often inaccessible data on the physiology of the fetus are well summarized in this small volume, *Physiology of the Fetus*,[15] of 249 pages. Among the more notable of the fifteen chapters are those on fetal blood, fetal circulation, fetal respiration, the genesis and function of the nervous system, and fetal endocrine glands. At the end of each chapter is a list of important references, mostly of recent date. The data presented are derived not only from observations on human and animal material, but also from the experimental results of many current investigators, among whom the author has played a leading role. Particularly stimulating is the presentation of controversial material, such as the discussion of fetal respiration. The evidence on both sides is well presented, and the author's conclusions logically drawn. In addition, suggestions are made regarding the possible course of future investigations. The book is not only an addition to the armamentarium of the embryologist, but should fill a great need for those specialists interested in the newborn infant and in the early neonatal period.

L. M. Hellman.

The collaboration of 34 authors with Drs. Holt and McIntosh in writing the eleventh edition of this classic textbook, *Holt's Diseases of Infancy and Childhood*,[16] is an innovation which permits an authoritative revision of the entire work. A successful attempt has been made to avoid the variegated style of the usual multiple-author textbook by the intimate collaboration of the specialists with the present editors in the revision of each section.

The new edition is 181 pages longer than its immediate predecessor. New topics discussed include, among others, cystic fibrosis of the pancreas, inclusion blenorrhea, petrositis, and regional enteritis. Particularly noteworthy is the increased length

[14]**Attaining Womanhood.** By George W. Corner, M.D., Professor of Anatomy, University of Rochester School of Medicine. 95 pages, illustrated. Harper & Brothers, New York, 1940.

[15]**Physiology of the Fetus.** By William Frederick Windle, Professor of Microscopic Anatomy, Northwestern University Medical School. 249 pages, illustrated. W. B. Saunders Company, Philadelphia, 1940.

[16]**Holt's Diseases of Infancy and Childhood.** By the late L. Emmett Holt and John Howland. Revised by L. Emmett Holt, Jr., M.D., Associate Professor of Pediatrics, Johns Hopkins University, etc. and Rustin McIntosh, M.D., Carpentier Professor of Pediatrics, Columbia University, New York, etc. Eleventh edition, 262 figures, 1,421 pages. D. Appleton-Century Company, New York, 1940.

of the sections devoted to growth, development, and psychopathologic problems of childhood. These changes are in step with modern pediatric teaching which places added emphasis on the norms for physical and mental health. The charts of normal osseous development are of particular value. The discussions of pathology, usually so inadequate in a general text, deserve special commendation. It is to be regretted that more adequate sections on such everyday problems as infantile colic and cryptorchidism were not substituted for the lengthier chapters dealing, for example, with the rare congenital disturbances of ossification. Space has been conserved in this edition by the elimination of the 153 separate chapters of the previous volume. This saving has permitted the inclusion of a vastly improved bibliography. The type, although smaller than previously, is darker and more easily read. Without reservation it can be said that this book continues to be the best pediatric textbook in the field.

Alfred S. Schwartz.

The appearance of the fifth edition of Faegre and Anderson's *Child Care and Training*[17] indicates a continuous and widespread interest in the training of young children, with a consequent demand for information regarding development and care. This book is a fine source of factual information regarding the growth and care of the normal child. The present edition has been revised to include what the authors regard as new or valuable contributions of recent years to the subject. A valuable help for lay parents is the series of well-considered questions at the end of each chapter, while for the teacher or physician the chapter bibliography offers suggestions for collateral reading or information on specific points. There are few families which would not benefit by reading this book.

Philip F. Williams.

The fact that this little book, *Getting Ready to Be a Mother,*[18] has run into a fourth edition is evidence of the avidity of the lay public for good books on health education. In revising Miss Van Blarcom's book, Miss Corbin has used photographs for the entire first chapter, illustrating different events in the life of the pregnant woman and the life of the newborn baby in its first few weeks after birth. These photographs depict adequate prematernity care. In the following eleven chapters, she has discussed in a lively fashion the different things which a pregnant woman should know. These chapters are illustrated with reproductions of plaster models of Dr. Dickinson which were displayed by the Maternity Center Association at the New York World's Fair. Throughout the book the expectant mother is urged to consult her physician regarding any uncertainties, disputed points, and abnormal symptoms. There is an excellent lecture on the care and training of the newborn baby and his minor complaints. The book closes with a very philosophical bit of advice to the new mother. Each book carries with it a large baby progress chart, convenient to file in the pocket of the book so that the mother may have a permanent record of her baby's growth.

The simple language and the excellent and profuse illustrations make this one of the best manuals on the subject.

Philip F. Williams.

Miscellaneous

The bête-noire of the laparotomists, *Foreign Bodies Left in the Abdomen,*[19] forms the subject of this volume in which the problem is handled from both the surgical

[17] **Child Care and Training.** By Marion L. Faegre, Assistant Professor of Parent Education, and John E. Anderson, Director of Institute of Child Welfare, University of Minnesota. Fifth edition, revised, 320 pages, illustrated. The University of Minnesota Press, Minneapolis, 1940.

[18] **Getting Ready to Be a Mother.** By Carolyn Conant Van Blarcom. Revised by Hazel Corbin, General Director of Maternity Center Association. Fourth edition, 190 pages, illustrated. The Macmillan Company, New York, 1940.

[19] **Foreign Bodies Left in the Abdomen.** The Surgical Problems and Legal Problems. By Harry Sturgeon Crossen, M.C., School of Medicine, Washington University, and David Frederic Crossen, LL.B., School of Law, Washington University, St. Louis. With 212 illustrations, including 4 color plates, 762 pages. The C. V. Mosby Company, St. Louis, 1940.

and legal angles. Dr. Harry Sturgeon Crossen in presenting the surgical problem tells why articles are lost and recounts in tabular analyses 250 sponge cases, with conditions found from the time of their loss until removal, in some instances the latter being as remote as twenty-four years. After giving detailed effects of a foreign body in the peritoneal cavity, he discusses the prevention of such accidents and describes what he considers the best and safest procedure, the continuous sponge system. Similar problems regarding instruments, drains and other foreign bodies lost in the abdomen, as well as foreign bodies left in other operations, are discussed in the light of cases reported by unfortunate surgeons. He discusses the differential diagnosis, the problems of swallowed objects, x-ray visibility diagnosis, and logical methods of treatment.

In the second half of the book David F. Crossen presents the legal side of such situations. Of importance to everyone who opens the abdominal cavity are the chapters on theory of defense in sponge cases, and the basis for estimating damages to the unlucky individual in whose body the foreign substances have been overlooked at the time of operation or in drainage.

There is no doubt that a perusal of this book which states definitely the responsibilities of the operating surgeon and the decision of jurists based on actual cases will occasion a consideration of methods of preventing such surgical problems. This book deserves a place in the libraries of all hospitals and of those surgeons who open abdominal cavities. The second, or legal, part of the book should be of great value to counsellors and attorneys who are attached to medical organizations or to medical defense insurance companies.

Philip F. Williams.

Rodney Maingot's two-volume *Abdominal Operations*[20] is an important contribution to surgery. Every aspect of abdominal surgery, except the genito-urinary and the genital tracts, is covered. The introductory chapter deals with abdominal incision, its selection, as well as the technique. The author scrubs for ten minutes, which appears rather long. A very careful discussion of disruption of abdominal wounds is given. Four hundred and fifty-eight pages are devoted to the stomach and duodenum. Particularly detailed are the indications, the choice of operation, and the reason for selecting various operations. This is kept up throughout the book and adds greatly to its value. The same applies to the careful discussion of the operative techniques themselves, the dangers to be looked for, and how to avoid accidents. In pyloric stenosis of infants, Maingot advises operation if a tumor is palpable. A very detailed pre- and postoperative dietary is to be commended. In resection of the stomach, he describes six modifications of Billroth I, and classifies Billroth II as anterior and posterior Polya partial gastrectomies. He favors partial gastrectomy as the operation of choice for chronic gastric ulcer. On the other hand, in acute perforations, simple suture, when practicable, is safest. For bleeding ulcer, early operation, opening of the stomach, transfixion sutures in the affected area are preferred to resection which is advised only in special cases.

Next come operations on the spleen. A special, short chapter by L. T. Bond on sternal puncture is included. For acute pancreatitis, after every diagnostic measure has been tried, he advises operation in all uncertain cases, and in a majority of severe cases seen within the first forty-eight hours.

Very excellent chapters on the surgery of the gall bladder and bile ducts conclude the first volume. Particular attention is paid to the anomalies of the hepatic and cystic arteries.

Volume II (the paging of the volumes is continuous) deals with the liver, including injuries, abscesses, neoplasms, cysts, and also cirrhosis. The varieties of omentopexy are taken up in detail for the latter condition. In the operation for appendicitis, the author is very conservative in appendicular conditions seen in the later stages. He accepts with reservation a condition of chronic appendicitis. A very complete description of peritonitis is given, including the treatment with chemotherapy. For the treatment of inguinal hernia, he completely rejects the use

[20] **Abdominal Operations.** By Rodney Maingot, Senior Surgeon to the South-End General Hospital, London, etc. In two volumes, 1,385 pages with 298 illustrations. D. Appleton-Century Company, New York, 1940.

of injections as a method of cure. All of the operations for hernia are described most adequately. More than two hundred pages are devoted to intestinal surgery which is covered minutely. The chapter on regional enteritis is excellent.

This book is one of the most detailed, clearly conceived and carried-out descriptions of abdominal surgery that has been published. It bespeaks an unusually large experience although the author quotes practically none of his own statistics. However, he does not hesitate to express a preference for certain types of treatment or operations. The illustrations, 298 in number, with several colored plates additionally, are of a high degree of excellence. The majority are halftones, beautifully executed but somewhat dark in tone. Individual figures, numbered as a single illustration, contain from five to ten steps, and consequently the actual number of illustrations which illuminate, are four or five times the number indicated. A considerable number of line drawings and excellent reproductions of radiograms are included. The world's literature is amply and accurately represented, the actual reference being given in brackets in the text. Consequently it is a pity that the publishers did not include an authors' index.

All in all, this treatise impresses me most favorably as a book of reference for description of the diseases dealt with, as well as a very valuable guide for surgeons, both for the minute descriptions in the text as well as the accompanying illustrations.

R. T. Frank.

This imposing volume of 1,280 pages on *Malignant Disease and Its Treatment by Radium*[21] by Cade is divided into three parts: The first part discusses the physics of radiation. The three chapters on teletherapy, dosimetry, and the measurement of radium plaques have been written by contributors who are outstanding in their interpretation of these considerations.

The second part of the book describes the biologic effect of radiation, and the various factors which influence radiosensitivity, such as embryologic development, variety of the type of cell, environment of the tumor and such physical facts as time, intensity, and previous irradiation are explained. The author discusses the various possible mechanisms in the mode of action of radium, not only describing the effect it has on physiologic activities of the tissues but subdivides the material to discuss excitation, inhibition, and destruction. Two chapters contrast the effect of this therapeutic agent on normal and malignant tissues; the latter chapter is amply illustrated, particularly, in regard to carcinoma of the cervix to show the time variations and effects of radium. A very practical chapter on dangers of radium not only includes measures to prevent damage to normal tissues, but also brings out the possibility of carcinogenesis as in skin cancer from radium dermatitis, and the necessary care to be exercised by hospital authorities in the handling of this element.

The third part of the book reflects the clinical experiences of the author with an enormous volume of malignant disease which has passed through his hands in the Westminster Hospital and Mount Vernon Hospital in England, as well as his experiences in the Radium Institute. In the opening chapter of this third part of the book, the author discusses the limitations of surgery and the value of and principles underlying radium treatment of cancer. He then proceeds to the detailed review of malignant disease of the various body systems, describing and discussing in a very clear, logical manner the life history of various systemic malignancies, their clinical grading, diagnosis, choice of method of treatment and technique which he and others have used, and the results of treatment in his hands, as well as in other medical centers. Of particular interest to the gynecologist should be the section of approximately eighty pages devoted to malignant disease of the uterus and other structures of the reproductive canal. The outstanding work on this subject by American gynecologists is reflected in a very large number of references to American literature on the subject of carcinoma of the cervix. He contrasts the technique of the Stockholm Radiumhemmet, Memorial Hospital

[21]**Malignant Disease and Its Treatment by Radium.** By Stanford Cade, F.R.C.S., Surgeon, Westminster Hospital, etc. 1,280 pages, 623 illustrations, many in color. Williams and Wilkins Company, Baltimore, 1940.

of New York, Paris Radium Institute with the technique used in the Mount Vernon Hospital in England. There is ample discussion of pre- and post-operative roentgen radiation not only here, but in an excellent section devoted to malignant diseases of the ovary. He states that in postoperative roentgen radiation in malignant disease of the ovary, using multiple ports of entry, treatment in four to five weeks, up to 6,000 r. to the pelvis, can be given without marked ill effects, and with only mild skin reactions.

This book is an outstanding contribution to the subject, both as a reference volume and as a practical manual for clinicians, radiologists, and pathologists. It should find a place in the libraries of all oncologists and hospitals. The book is profusely illustrated, with many color plates, and has extensive chapter bibliographies. It is an excellent example of the bookmaker's art.

Philip F. Williams.

Sex in Development[22] is a study of the growth and development of the emotional and sexual aspects of personality together with physiologic, anatomic, and medical information on a group of 153 normal women and 142 female psychiatric patients.

The work is that of a considerable number of investigators, edited by Dr. Carney Landis. The authors are well aware that they "have attempted to be objective in dealing with data based on emotionality and feeling concerning which it is difficult to be objective." Their attitude in this study has been that of empirical scientists without any attempt to prove or disprove any theory or to set up their own theories or hypothesis. Their work has been the synthesis of biographic sketches based on a controlled interview (in contradistinction to the uncontrolled psychoanalytic approach); marriage inventory; general information inventory; physical examination; vocation interest blank for women; roentgenologic studies of the pelvis; and psychiatric case history. They are well aware that the experimental psychologist will object to findings acceptable to the analyst, and vice versa.

Whether one is in agreement or disagreement with the technique used, no one can say that the approach has not been careful, thorough, and unbiased. The results, as the authors themselves realize, are not final and will be acceptable or unacceptable, depending upon the bias of the reader. They find that psychosexuality has its origin long before puberty. They likewise find that sexual aggression before puberty may be followed by homoerotic trends in adult life. They emphasize that the "most important" problem which the girl faces in adolescence is that of freeing herself from her family ties. Approximately one-sixth of the group was markedly narcissistic, about one-fourth showed some degree of masculine protest. In the abnormal group, extreme narcissism was associated with an obsessive interest in sex. They agree that surprisingly few anatomic or physiologic differences were noted between normal women and women suffering from functional mental disorders. In the psychotic groups, hypoplastic body form was more often noted. In normal women, 47 per cent of poor marital sex adjustment occurred in the group having anthropoid pelves and in only 10 per cent of the gynecoid type. They conclude that normality can and does exist over a much wider range of developmental variation than has been thought. This interesting monograph concludes with all of the information forms used and with a tabulation of the data. It can and should be read with interest by all to whom this problem is of importance, irrespective of the reaction which it may produce.

R. T. Frank.

This research study, *Physiology of Micturition*,[23] by Langworthy, Kolb and Lewis should be of special interest to the gynecologist, for to him the primary

[22]**Sex in Development.** Edited by Carney Landis, Associate Professor of Psychology, Columbia University; Principal Research Psychologist, Psychiatric Institute and Hospital. 329 pages. Paul B. Hoeber, Inc., New York, 1940.

[23]**Physiology of Micturition.** By Orthello R. Langworthy, Lawrence C. Kolb, and Lloyd G. Lewis, Sub-Department of Neurology, and James Buchanan Brady Urological Institute of Johns Hopkins University. 232 pages, illustrated. Williams & Wilkins Company, Baltimore, 1940.

symptoms of disturbances of micturition are presented so frequently. This experimental and clinical study concerns the innervation of this smooth muscle cavity. The relation of the physiology of the bladder to lesions of the peripheral nerves, spinal cord, and brain has been investigated, discussed, and summarized. The authors point out that from their studies it seems apparent that changes occur in the bladder of pregnant women similar to those which have been observed in the ureter in pregnancy. They conclude that the increased volume of the bladder in pregnancy is dependent upon the action of progestin. The influence of various analgesic and anesthetic agents on micturition is discussed. The section on clinical diagnosis lists illustrative cases in which disturbance has been caused by lesions of the central nervous system and various neurologic diseases.

Philip F. Williams.

When, in his introduction, an author states that his book as it appears in print is not to his entire satisfaction and when further he invites constructive criticism, he at once disarms the critic and one must read his book in the light of his modesty. However no apologies are needed by an author who possesses the scholarship shown in this book, *Bacillary and Rickettsial Infections.*[24]

Dr. Holmes tells us that here he has presented a book for medical students, setting forth the subject matter as he would wish it given to the student. The book covers only a limited portion of the field of the communicable diseases (not touching upon the diseases caused by viruses or by the pathogenic cocci). It runs to 630 pages of text. It contains the subject matter covered in one quarter of the course in didactic medicine at Northwestern University Medical School. It may be questioned whether the medical student can actually digest the material presented within this volume, in view of the impact of other fields which compete for his attention and must be mastered. If the student absorbs only half of the material, he will be a well-educated physician. However, if we look upon the book of Dr. Holmes as a contribution to the field of medical literature rather than purely as a textbook, we can have little to criticize.

The majority of the diseases discussed are approached historically. The history of the occurrence of the disease, the names, and the pertinent contributions of those who in the past wrote about the condition serve as fascinating introductions; therefore when the etiology, symptomatology, treatment, etc., are discussed, the disease already has a familiar aspect; and there are many points that offer possibilities for association. The usual formal presentation is not slighted and has greater interest coming as it does as a sequence to the introductory discussion.

There are interest and stimulation to be obtained in reading the pages of this book. There is evidence of wide knowledge and long and painstaking study by the author without pedantic presentation.

Moyer S. Fleisher.

Goodman and Gilman's *The Pharmacological Basis of Therapeutics*[25] is, in the best sense of the word, a textbook of pharmacology, toxicology, and therapeutics. Its content is far too encyclopedic to permit of detailed review; its scope embraces anatomy and chemistry also. The book is designed for physicians and students; its appeal, however, should include investigators in all branches of science.

The arrangement is admirable—central nervous depressants and stimulants, local anesthetics, drugs acting on autonomic effector cells, cardiovascular drugs, etc.; drugs acting locally on the skin and mucous membranes; antiseptics, disinfectants and drugs used in chemotherapy of infectious diseases, drugs of endocrine origin and the vitamins are sections here selected for comment because of their impor-

[24] **Bacillary and Rickettsial Infections. Acute and Chronic.** By William H. Holmes, Professor of Medicine, Northwestern University Medical School, Chicago, etc. 676 pages. The Macmillan Company, New York, 1940.

[25] **The Pharmacological Basis of Therapeutics.** By Louis Goodman, M.A., M.D., Assistant Professor of Pharmacology and Toxicology, Yale University, School of Medicine, and Alfred Gilman, Ph.D., Assistant Professor of Pharmacology and Toxicology, Yale University, School of Medicine. 126 figures, 1,383 pages. The Macmillan Company, New York, 1941.

tance. The chapters devoted to sulfanilamide and related sulfamide drugs are excellent, clear, and concise as is the entire text of the book. In the 73 pages devoted to the endocrines, a large amount of information, a lucid, comprehensive summary and an unbiased presentation are given.

Each chapter contains the essential historical, chemical, and physiologic basis in addition to the detailed presentation of the pharmacology, frequently illustrated by fundamental experiments. The therapy throughout is sound and conservative. The chapter bibliographies are short but comprehensive. A short chapter on prescription writing concludes the volume. In spite of the huge amount of data, the text is clear, readable, interesting and not in any way ponderous. This is a very valuable contribution with wide appeal and utility.

R. T. Frank.

This *Cyclopedic Medical Dictionary*[26] really is an entirely new publication and not merely a revision of Taber's previously published *Digest of Medical Terms.* It contains 1,500 pages of dictionary material with between 50,000 and 60,000 words. There are included several new features, not found in other medical dictionaries, as e.g., 16 pages, entitled "The Interpreter," of questions and terms applying chiefly to diagnosis which are given in the following five languages: English, French, German, Italian, and Spanish.

Taking its place somewhere between the large standard medical dictionary and the small, concise book prepared for nurses, Taber's dictionary should prove useful to physicians and medical students as well as to nurses.

Hugo Ehrenfest.

The rapid increase in new drugs offered on the market and far-reaching changes in endocrinologic and biologic methods of treatment have created a definite demand for a thoroughly revised and enlarged edition of the *Modern Drug Encyclopedia.*[27] Except for the official publication containing only those pharmaceutic products approved of by the Council on Pharmacy of the A. M. A., there is no other competent and complete source available but this Encyclopedia for authoritative information in regard to chemical constitution, action, uses, dosage, advantages or objectionable by effects of the many drugs, widely used, for oral, hypodermic, intramuscular, intravenous, vaginal and rectal application. The convenient arrangement of this immense amount of useful information has been only slightly changed in the new edition. Physician, dentist, pharmacist, and medical student, as well, will find this volume most useful in their work.

Hugo Ehrenfest.

With the aid of nine collaborators, each a recognized authority in a special field of physiology, Bard presents Macleod's famous work on *Physiology in Modern Medicine*[28] in a largely rewritten ninth edition. Although several new chapters have been added, others have been combined; therefore the total number has not been increased.

This volume necessarily contains much information of interest and practical importance to obstetricians and gynecologists. In particular we may refer to chapters dealing respectively with the hypophysis, the ovary, and endocrine factors in reproduction (menstruation, pregnancy, lactation, menopause, and sterility). As in previous editions the bibliography of each of the major sections is placed at the end of the volume. The index has been enlarged.

Hugo Ehrenfest.

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[26]**Taber's Cyclopedic Medical Dictionary.** By Clarence Wilbur Taber, and Associates. Illustrated. F. A. Davis Company, Philadelphia, 1940.

[27]**Modern Drug Encyclopedia. Therapeutic Guide.** By Jacob Gutman, M.D., Phar.D., F.A.C.P., Director, Brooklyn Diagnostic Institute, etc. Second edition, 1,644 pages. Published by New Modern Drugs, New York City, 1941.

[28]**Macleod's Physiology in Modern Medicine.** Edited by Philip Bard, Professor of Physiology, Johns Hopkins School of Medicine. Ninth edition, 387 figures, 1,256 pages. The C. V. Mosby Company, St. Louis, 1941.

L. Emmett Holt, Pioneer of a Children's Century[29] was both an idealist and a man of action. In this delightfully written story of his life by Mr. Duffus and Dr. Holt, Jr., one learns of Holt's decision to study medicine, his various experiences in anatomy, surgery, and general practice until he ended up in his final choice of children's diseases. From that point on there was hardly a step in the development of American pediatrics in which he did not take an active part—the establishment of the Babies Hospital; publication of his two books, one for the laity and one for the physician, both best sellers; his influence in helping to establish the Rockefeller Institute; his association with the Milk Situation; all are beautifully described. His contacts with laboratory, research, literature, national problems, post-war situations in Europe, and medical organizations show what a tremendous vitality this man possessed. Letters which he wrote from China just before his death reveal that his intense interest in the problems of children kept up until the last minute. This is a fine example of medical biography.

Philip F. Williams.

In the evening of a long and useful life, Dr. Wolf recounts his early days in Germany and his practice in Kansas City in a most interesting medical biography entitled *A Family Doctor's Notebook*.[30] The recollections of a man who at seventy-five years looks back over some fifty years of practice and thirty-five years of teaching not only makes an interesting history of the practice of medicine in the United States, but gives many personal opinions of the social trend in the present and past decades. Dr. Wolf has well described the place of the physician in relation to the patient, his brother physician and civic activities. Among his philosophic essays on present-day topics are two interesting chapters on the high cost of doctoring and medical economics in which Dr. Wolf very ably pleads the case for the physician. He closes the book with a chapter which reflects pride in the past accomplishments of the medical profession while looking forward to greater discoveries of future days. These observations and essays merit wide reading by physician and layman.

Philip F. Williams.

Dr. Minnitt has taken over the revision of this book *Ross and Fairlie's Handbook of Anaesthetics*,[31] upon the deaths of the former authors. Much of the material in this fifth edition is stated to have been re-written, while three additional chapters have been added. The first one is on "Cyclopropane and Closed Circuit CO_2 Absorption Anaesthesia." The second new chapter is devoted to the "Therapeutic Use of Oxygen, Helium, and Carbon Dioxide" and in this chapter, particularly, there occurs the discussion of treatment of postoperative complications by these agents, as well as the use of oxygen tents.

In discussing anesthesia in obstetrics, Dr. Minnitt recounts his personal experiences with chloroform, which is not largely used in the United States. He gives an excellent recapitulation of various methods for producing amnesia and analgesia during labor, and describes an apparatus for the use of gas analgesia in the home labors. He advocates a wider employment of local anesthesia for cesarean section, and the avoidance of chloroform for the major vaginal operations. This compact presentation of the subject should be a useful guide to students and practitioners of anesthesia.

Philip F. Williams.

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[29] **L. Emmett Holt, Pioneer of Children's Century.** By R. L. Duffus and L. Emmett Holt, Jr. Foreword by Edwards A. Park, Professor of Pediatrics, Johns Hopkins University. Illustrated, 295 pages. D. Appleton-Century Company, New York, 1940.

[30] **A Family Doctor's Notebook.** By I. J. Wolf, M.D., Professor of Medicine, Emerit. University of Kansas School of Medicine. Fortuny's, New York City, 1941.

[31] **Handbook of Anaesthetics.** Revised by R. J. Minnitt, M.D., Lecturer in Anaesthesia, University of Liverpool, etc. With chapters on local and spinal anaesthesia by W. Quarry Wood, M.D., Surgeon, Edinburgh Royal Infirmary. Fifth edition, 103 illustrations, 364 pages. Williams and Wilkins Company, Baltimore, 1940.

Sammartino[32] practices dilatation of the sphincter ani with one, two, or more fingers preliminary to abdominal palpation in inflammatory and other acute and chronic conditions of the abdomen. By this measure he claims to facilitate localization and diagnosis. His claims are based on the study of 400 cases of various abdominal diseases.

R. T. Frank.

The third series of Surgical Monographs by Branco Ribeiro[33] deals with diverse surgical subjects. Of interest to our readers are a report on appendicitis during pregnancy (report of one case, considerable statistical literature). Also a report of large uterine myoma (weight 13 kg.).

R. T. Frank.

Zuckermann in his *Surgical Treatment of Constipation*[34] appears to be a disciple of Lane. He concedes that the majority of patients should be treated by hygienic, dietetic, physiotherapeutic, and drug measures. Surgery should be limited to persistent, rebellious forms in which the radiographs show marked retardation of the fecal column and to patients in whom toxemia and pain are manifest. Such measures as colopexy, various entero- and coloanastomoses are described most sketchily. His main theme, however, is abdominal ganglionectomy which he depicts in detail. The literature from 1923 to 1936 is given in abstracts. The histories of twenty patients on whom various types of ganglionectomies were performed by the author, form the main text.

R. T. Frank.

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[32]**La Maniobra Ano Parieto-Abdominal En Los Procesos Agudos Del Abdomen.** Por Dr. Emilio S. Sammartino. El Ateneo, liberia y editorial. Buenos Aires, 1940.

[33]**Estudos Cirurgicos.** By Eurico Branco Ribeiro, Director do Sanatorio São Lucas. 219 pages, illustrated. Sociedade Editora Medica Limitada, São Paulo, Brasil, 1940.

[34]**Cirugia de la Constipacion.** Par el Dr. Conrado Zuckermann, Professor de patologia quirurgica de la faculdad de medicina de Mexico. Con 32 grabados. Mexico, 1939.

Society Transactions

SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS

THIRD ANNUAL MEETING, JACKSONVILLE, FLA.
FEBRUARY 7 AND 8, 1941

The following papers were presented:

Placenta Bilobata. Drs. Richard Torpin, Augusta, Ga., and B. F. Hart, Winter Park, Fla. (For original article, see page 38.)

Sterilization in the Puerperium. Drs. W. N. Thornton, Jr., and T. J. Williams, University, Va. (For original article, see page 54.)

Benjamin Rush, Obstetrician. Dr. M. Pierce Rucker (President's Address) Richmond, Va.

Placenta in Late Toxemia of Pregnancy. Dr. R. A. Bartholomew, Atlanta, Ga.

Acute Polyhydramnios. Dr. J. D. Parker, Greenville, S. C.

Acute Appendicitis in Pregnancy. Dr. C. D. Hoffman, Orlando, Fla.

The Excretion of Estrogenic and Androgenic Substances by Intra-Human Primates. Dr. William C. Young, New Haven, Conn.

The Role of the Maternity Home in Treating the Low Income Group. Dr. J. M. Hoffman, Pensacola, Fla.

Supravaginal and Total Hysterectomy. Dr. Richard L. Pearse, Durham, N. C. (For original article, see page 22.)

A Study of 150 Consecutive Cases of Ectopic Pregnancy. Dr. H. H. Ware, Jr., and W. C. Winn, Richmond, Va. (For original article, see page 33.)

Oral Progestin (Anhydro-Hydroxy-Progesterone) in the Treatment of Dysmenorrhea. R. B. Greenblatt, E. McCall, and R. Torpin, Augusta, Ga. (For original article, see page 50.)

The guest speakers were Dr. John Rock, Boston, Mass.; Dr. William C. Young, New Haven, Conn.; and Dr. N. J. Eastman, Baltimore, Md.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Cesarean Section

Heard, Kenneth M.: Anesthesia in Cesarean Section, Surg., Gynec. & Obst. 70: 657, 1940.

In the literature on cesarean section, very little mention is made of the anesthetic and even less of its effect upon the respirations of the infant. When artificial respiration is needed or pneumonia follows initial respiratory difficulties, it is too often dismissed as due to toxemia or other ill health in the mother. In reality, the type of anesthetic used for the operation plays a very definite part in the baby's start in life. No form of anesthesia nor method of resuscitation will save a baby with a very marked defect of brain or heart. It is doomed by congenital defects for which there is no remedy. Many others, however, fail to survive the first few hours because their respiratory mechanism is unable to function properly, due to depression by an anesthetic or sedative. It is impossible to anesthetize or sedate the mother by inhalation or narcotics without anesthetizing the fetus. The drug is absorbed at the time when the fetal respiratory and cardiac centers are at their lowest ebb, following prolonged labor or damage secondary to maternal ill health. Most babies, particularly if the operation is at the time of election, will withstand this terminal depression and breathe spontaneously. The occasional one, however, is unable to cope with the depressing effect of the anesthetic and breathes only after resuscitation. Too often the respirations remain unsatisfactory, and atelectasis leads to pneumonia or death. Since it is impossible to predict in advance the exact state of the respiratory system, safety demands the use of the anesthetic which will add least strain to the already overburdened fetus. The anesthesia in question in this series proved to be spinal with straight cyclopropane-oxygen, or nitrous oxide-oxygen without ether a close second. Ether is definitely contraindicated, particularly after a heavy sedative.

WILLIAM C. HENSKE.

Synephias, M.: Spinal Anesthesia With Percain and Cesarean Section, Rev. franç. de gynéc. et d'obst. 34: 162, 1939.

During the past three years, 67 cesarean sections were performed at the Strasbourg Clinic under spinal anesthesia with percaine and 19 additional cesareans were done under ether anesthesia. Synephias compares the three forms of anesthesia used for cesarean section, namely, general, local, and spinal.

Among the general anesthetics used are ether, evipan, and gas. Ether is toxic, it produces disagreeable postoperative effects, and it may be harmful to the child. Evipan has resulted in many accidental deaths. Thus, Menegaux reported 22 deaths and Synephias collected six serious accidents and 20 deaths during short operations performed under evipan. Danger to the fetus is not excluded because of the permeability of the placenta to the barbiturates.

Gas in the form of nitrous oxide, ethylene, and cyclopropane is a distinct advance in general anesthesia, because in over 4,000,000 gas anesthesias there has not been a single death. However, gas anesthesia requires cumbersome and expensive apparatus and the services of a special anesthetist. Furthermore, they are explosive and they have a bad effect on the contractility of the uterus.

Local anesthesia is excellent and innocuous, but it is painful when used in women who are having violent uterine contractions. It is practically useless in cases of cesarean section where the uterus is exteriorized.

Spinal anesthesia is simple, it has a favorable action on uterine contractions and therefore diminishes bleeding, it permits easy exteriorization of the uterus and has no harmful effect on the child. However, it may be dangerous, because spinal anesthesia increases in risk the nearer a pregnant woman is to term.

J. P. GREENHILL.

Feldweg, P.: The Position of Cesarean Section in Obstetrics, Zentralbl. f. Gynäk. 63: 1511, 1939.

The cesarean section results for the last five years in the author's clinic are studied and reported. There were 205 sections and about 3,300 deliveries from below, with no maternal section deaths but with 8 fetal deaths. These results are then compared with those of delivery from below. When other than spontaneous delivery occurred, but where delivery was accomplished from below, there was a maternal mortality of 1.32 per cent, comparable to the expected mortality of cesarean section. A brief summary of the histories of the patients who died after delivery from below leaves no doubt but that cesarean section was either not indicated or would not have changed the outcome. The author concludes that, as it is applied in his clinic, an extension of the indications for section from the standpoint of the welfare of the mother is not justified.

He then examines the fetal mortality. Spontaneous delivery, operative delivery from below, and section carried 2.9 per cent, 13.9 per cent, and 3.8 per cent fetal mortality, respectively. The cesarean section mortality is weighted with several mistaken diagnoses (fetal abnormality, unrecognized prematurity, etc.) which lead him to believe that this can be reduced. He concludes that some extension of cesarean section on the basis of fetal welfare is justified, particularly in view of the very low maternal mortality of the operation. Against this, he places what he believes to be a lowered fertility rate in patients upon whom section has been done.

The indications for section are those generally accepted so far as can be determined from the brief statements. Two of these will not find acceptance however. Eclampsia and previous section accounted for more than 50 of the reported operations. No section is done after a vaginal examination of any sort and whether done in his own clinic or elsewhere. All of his sections are done under local anesthesia, and he makes a strong plea for this procedure. A transverse uterine incision is made without elevating the bladder.

As in all German clinics, the author has given much consideration to the problem of embolism. It will perhaps be a shock to most physicians in this country to read that the patient is made to get up from the operating table and walk. Every day thereafter the patient is gotten up and walks. No bad results have been seen (Pfannenstiel's incision of the abdominal wall is used), and there were no embolus deaths in the series.

In conclusion, the author lays down five rules which are the most important factors in cesarean section results. These are worth repeating.

1. Exclusion of all infected patients, as well as those who have had vaginal operations or vaginal examinations (presumably during labor).
2. Avoidance of all alkaloids (before delivery of the child) and all anesthetic agents which have a central effect.
3. The use of only local anesthesia.
4. Transverse incision of the abdominal wall and curved transverse incision of the uterus.
5. Get the patient up and about from the operating table and every day thereafter.

Some of the statements will not find general agreement in this country, but the paper gives one the impression of a clear-headed presentation of the problem and will repay reading in the original.

J. L. MCKELVEY.

Weaver, R. T.: Changing Conditions for Cesarean Section, Canad. M. A. J. **40:** 259, 1939.

A review of the literature reveals a wide variation in the incidence of cesarean section with a definite tendency toward an increase. In some areas, 33 per cent of maternal deaths have occurred following cesarean section delivery. In 4,694 cases collected from the literature, the indications for operation were as follows: cephalopelvic disproportion, 44.6 per cent; previous section, 15.2 per cent; placenta previa, 6.6 per cent; accidental hemorrhage, 2.9 per cent; late toxemias, 9.1 per cent; cardiac disease, 3.9 per cent; and miscellaneous, 12.0 per cent.

A discussion of these indications shows that there are considerable differences of opinion among various authors. Weaver believes that cesarean section must be looked upon as the most dangerous of all abdominopelvic operations and that the nursing and medical professions and the public must realize that abdominal delivery is not the solution for every obstetric problem.

CARL P. HUBER.

Howkins, John: Pelvimetry and the True Conjugate, Brit. M. J. **1:** 278, 1938.

The author feels that cesarean sections are recommended, too often, on the basis of the often erroneous conclusion that, if the sacral promontory can be felt per vaginam, the patient has a contracted pelvis. He explains that three factors have to be taken into account, namely, first, the length of the true conjugate; second, the effective length of the examining finger; and, third, the rigidity of the vaginal introitus, which depends largely upon the cooperative relaxation of the patient and on her parity.

He concludes that clinical measurement of the true conjugate can be done in normally sized pelves when good cooperation is obtained and the examiner has had practice and is skillful. He also points out that when the diameter is truthfully obtained it is open to considerable error in addition to that due to the particular anatomy of a given patient, such as the depth and inclination of the symphysis.

F. L. ADAIR AND JOHN A. HAUGEN.

Johnston, H. W.: The Termination of Pregnancy Before the Period of Viability by Abdominal Hysterotomy Through the Lower Uterine Segment, Canad. M. A. J. **43:** 552, 1940.

The premature termination of pregnancy after the third month by abdominal hysterotomy through the lower uterine segment is described. The author prefers this procedure because the incision is covered by the peritoneum of the bladder flap and adhesions which may follow the usual high incision are prevented. The uterine incision may be made either longitudinally or transversely.

CARL P. HUBER.

Anderodias, J., and Pery, G.: The Indications for Low Cesarean Section in Amniotic Infections, Rev. franç. de gynéc. et d'obst. **34:** 1, 1939.

The purpose of this paper is to show that the low cervical cesarean section may be performed in cases which formerly would have been subjected to multilating operations. Among 85 instances there were five fatal cases where the membranes had ruptured some time before the operation (6, 8, 8, 46, and 48 hours, respectively). The longer the bag of waters was ruptured the greater the risk of the operation.

In cases of definite amniotic infection, the authors employ the low operation but they sew the abdominal wall in one layer instead of three. They claim by this measure to avoid dead spaces which would be filled by hematomas which become infected and produce abscesses of the abdominal wall. Among 15 patients operated upon in this way, there were no failures.

Among the 83 women operated upon while they had a temperature above 37.5° C., there were 5 deaths (5.8 per cent). The causes of death were septicemia (2), peritonitis, cellulitis of the broad ligament and myocarditis. Infections manifested

themselves after operation in 22 cases and consisted of the following: unilateral phlebitis (6), bilateral phlebitis (2), abscess of abdominal wall (6), pulmonary complications (5), and endometritis (3). The total fetal mortality was 7 per cent.

During the last ten years, the total number of cesarean sections performed was 280. There were 9 maternal deaths, an incidence of 3.2 per cent.

J. P. GREENHILL.

Lorier, V. L.: My Experience With the Cesarean Operation, Rev. franç. de gynéc. et d'obst. **34**: 285, 1939.

This paper is based on 277 cesarean sections performed in the author's clinic. Of this number 11 were classic cesarean sections and 166 were cervical operations. Among the classic cesarean cases the death rate was 9 per cent; whereas in the cervical group it was only 3.6 per cent. In the group of classic operations, the maternal mortality was 3.9 per cent for the patients with intact membranes, but it was 16 per cent for those with ruptured membranes. In the low cervical group, the figures were 5.1 and 5.7 per cent, respectively. The fetal death rate for the classic sections was 5.4 per cent and for the low operations it was 4.8 per cent. The author believes that the low cervical operation is the one of choice.

J. P. GREENHILL.

Courtois, J., and Bouchacourt, C.: Concerning 158 Low Cesarean Sections. Indications and Results, and Opportune Time for Operating, Rev. franç. de gynéc. et d'obst. **33**: 790, 1938.

In a series of 205 cesarean sections performed by Courtois and Bouchacourt, 158 were of the low cervical type. The indication in 113 cases was contracted pelvis, and in this group there were 7 maternal deaths (6.19 per cent) and five fetal deaths (4.42 per cent). Among the remaining 45 cervical operations performed for a variety of indications, there were three maternal fatalities (6.8 per cent). Hence, the total maternal mortality was 6.32 per cent and the total fetal death rate was 5.06 per cent. In this series there were 16 low cervical operations in women who were more or less infected and the death rate in this group was 18.7 per cent. On the other hand, the death rate in the clean cases was only 3.5 per cent. The maternal mortality for the patients not in labor was 6.25 per cent; for those at the beginning of labor, it was 2.94 per cent; for those late in labor, it was 10 per cent; and for a few in whom the operation was performed after a very long labor, it was 33.3 per cent.

The authors conclude that the optimum time for performing a cesarean section is at the beginning of labor, because at this time the best results for both mother and baby are obtained. It is preferable to operate shortly after the bag of waters has ruptured. For the mother, the twentieth hour of labor is a dramatic pivotal point, because after this the risks of the operation increase very markedly. Infants have less resistance than their mothers; hence, in cases of dystocia, the tenth hour should be considered the dead line, especially if the membranes have ruptured. The low cervical cesarean section has a distinct maternal mortality regardless of the indication, the condition of the mother and the skill of the operator.

J. P. GREENHILL.

Serdukoff, M. G.: Advantages of the Transverse, Transcervical and Retrovesical Incision in Cesarean Section, Gynécologie **38**: 463, 1939.

In the opinion of Serdukoff, the lower uterine segment is far preferable to the body of the uterus for making the incision in cesarean section. The transverse incision in the lower uterine segment has the following advantages over the vertical incision: The risk of interstitial hemorrhage is less; the coaptation of the tissues is more perfect; the scar heals better because the lower uterine segment is at rest; there is better peritonization which is important in the prevention of adhesions; the obstetrician has more room for the extraction of the fetus; the uterus is opened

without exteriorization; the intestines are not in contact with the field of operation and the operation may be performed by any physician who can do surgery.

J. P. GREENHILL.

Fuchs, H.: Labor After Cesarean Section, Particularly After the Arc Incision in the Isthmus, Zentralbl. f. Gynäk. **61**: 2578, 1937.

In the 245 cases of low cesarean section performed, the maternal mortality was 1.6 per cent. In this group 46 women were subsequently delivered by cesarean section, but 19 had vaginal deliveries. There was no mortality in this group. At the time of the repeated cesarean operation, the scar was carefully examined. In 33 cases no scar was visible, in 10 there was a slight thinning of the scar area, and in 3 cases there was a pathologic thinning. In 5 cases pieces of tissue were removed for microscopic examination. The author believes that the danger of rupture of the uterus after the low operation is considerably less than after the classic operation. Nevertheless even women who have cervical operations must be carefully watched in subsequent labors because the scar may thin out and rupture subperitoneally.

The author recommends that in all subsequent cesarean sections, the operator should carefully inspect the area of the previous scar and correlate it with the stage of labor. He should also remove a piece of tissue for histologic study. The only investigation reported of the histologic study of uterine scars after cervical cesarean sections is that of Greenhill and Bloom. More such studies are needed. The author also suggests that in cases of vaginal delivery after cesarean section, the physician should examine the isthmus of the uterus.

J. P. GREENHILL.

Repetti, Mario: Strength of the Uterine Scar Following Cesarean Section, Folia demograph.-gynaec. **37**: 159, 1940.

The author describes a case of spontaneous rupture of the uterus in the beginning of labor in a woman who had had two previous cesarean sections. One was of the fundal type and the other in the lower segment. The rupture occurred in the first fundal incision where the placenta had attached. The writer discusses the frequency, etiology, pathogenesis, and pathology of rupture of the uterus following previous cesarean section. In general, authors prefer the lower segment incision. In conclusion, it is the writer's opinion that even in the absence of any sign of abnormality in the puerperium, whether the incision was fundal or segmental, one cannot prognosticate as to whether the scar will hold or not.

MARIO A. CASTALLO.

Nicoletti, Guido: The Fate of the Cesarean Section Scar, Rassegna d'ostet. e ginec. **48**: 165, 1939.

The author describes the histology of a uterine scar one year after cesarean section. At this time the uterus was removed with the adnexa because of ovarian malignancy.

The author states that the uterine wounds of cesarean sections heal only by secondary intention. The best prophylaxis to good uterine scar formation is dependent upon the accuracy of the anatomic reconstruction of the uterine wound. A poorly reconstructed uterine wound in the fundal region will logically be more liable to rupture from the less well-formed scar.

CLAIR E. FOLSOME.

Rickards, C. E. B.: Uterine Rupture Following Caesarean Section, Brit. M. J. **1**: 1359, 1938.

Rupture of the uterus following a previous cesarean section may occur during pregnancy or during labor, especially if the latter is obstructed. The author classifies such ruptures into five groups, and furnishes case histories and characteristics of each group.

All patients who have had a previous cesarean section should have subsequent confinements under skilled supervision and have access to a fully equipped operating theater. If the indication for cesarean section is absolute, the operation should be performed during the last week of pregnancy or at the onset of labor. Unnecessary delay in these cases may lead to rupture of the uterus. The patient must be carefully supervised during the latter part of pregnancy and abnormal symptoms, i.e., lower abdominal pain, must be regarded with suspicion.

F. L. ADAIR AND S. A. PEARL.

Fournier, R.: Insurmountable Dystocia Caused by a Scar of a Transverse Low Cesarean Section, Gynécologie **38**: 5, 1939.

The incidence of rupture of the uterus following the cervical cesarean section in which the longitudinal incision is used is about 0.28 per cent. The scar itself does not produce any dystocia during labor. On the other hand, Fournier reports a case of cervical cesarean section in which a transverse incision was used. In this case, the well-healed scar produced such serious obstruction to the descent of the fetal head that a rupture would certainly have occurred in the lower uterine segment if a hysterectomy had not been performed. At operation, after opening the uterus, a thick shelf of muscle was found preventing descent of the head. This was in the region of the transverse incision of the low cesarean section. After removal of the baby, the uterus contracted, and it was seen that the previous scar divided the uterus into two parts, a lower part with a thin, flaccid wall and an upper part with a very thick wall about three times the thickness of the lower part. There was no transition between the two parts but a sudden sharp change.

J. P. GREENHILL.

Arthure, H.: Rupture of a Cesarean Scar Treated by Simple Drainage and Followed by Pregnancy, Lancet **2**: 19, 1938.

A case is reported in which unrecognized rupture of a classical cesarean scar occurred during the thirty-sixth week of pregnancy with extrusion of the fetus into the abdomen. Ten weeks later, following attempts at bougie induction of labor, laparotomy was performed. The macerated extrauterine fetus, lying anterior to a rupture in the uterus, was removed and the wound drained. Two years later in a subsequent pregnancy, laparohysterotomy and sterilization were performed. The site of rupture could not be seen, and there was only one omental adhesion to the uterus.

The author has been unable to find other reports of pregnancy subsequent to rupture of the uterus which was treated by drainage.

CARL P. HUBER.

Items

American Board of Obstetrics and Gynecology

The next written examination and review of case histories (Part I) for Group B candidates will be held in various cities of the United States and Canada on Saturday, January 3, 1942, at 2:00 P.M. Candidates who successfully complete the Part I examinations proceed automatically to the Part II examinations held later in the year.

Applications for admission to Group B, Part I examinations must be on file in the Secretary's Office not later than October 6, 1941. Group A applications must be received in the Secretary's Office not later than March 1, 1942.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Atlantic City, N. J., immediately prior to the 1942 meeting of the American Medical Association.

As previously announced in the Board booklet, this fiscal year (1941-1942) of the Board marks the close of the two groups of classification of applicants for examination. Thereafter, the Board will have only one classification of candidates, and all will be required to take the Part I and Part II examinations.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

Candidates certified (total 227) by American Board of Obstetrics and Gynecology at the June, 1941, meeting held at Cleveland, Ohio:

ARCHIE A. ABRAMS, Boston, Mass.
GERHARD AHNQUIST, New York, N. Y.
RUDOLPH F. AMYOT, Cohoes, N. Y.
I. ANDRUSSIER, Philadelphia, Pa.
J. MARSH ALESBURY, Philadelphia, Pa.
B. R. AUSTIN, Pittsburgh, Pa.
JOHN M. BAILEY, Evanston, Ill.
D. M. BALDWIN, Jacksonville, Fla.
GEMMA BARZILAI, New York, N. Y.
D. S. BAYER, Nashville, Tenn.
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JERRELL BENNETT, Fort Worth, Tex.
JAMES BERCEY, Milwaukee, Wis.
SAUL BERMAN, Boston, Mass.
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WILLIAM T. BLACK, JR., Memphis, Tenn.
ROY V. BOEDEKER, St. Louis, Mo.
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HARRY BENARON, Chicago, Ill.
JAMES P. BOYLAN, New York, N. Y.
PETER L. BOYLE, Youngstown, Ohio
HARRY BOYSEN, Chicago, Ill.
P. N. BRAY, Duluth, Minn.
JAMES X. BREMNER, Chicago, Ill.
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WILLIAM H. BROWNFIELD, Los Angeles, Calif.
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NANCY D. CAMPBELL, Las Vegas, N. M.
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BENJ. B. WETCHLER, Fort Bragg, N. C.
JOHN WHITRIDGE, JR., Baltimore, Md.
S. W. WILLIS, Bronxville, N. Y.
LEO WILSON, New York, N. Y.
MAUDE HALL WINNETT, Chicago, Ill.

The Second American Congress on Obstetrics and Gynecology

The Second American Congress on Obstetrics and Gynecology will be held in St. Louis, Missouri, April 6 to 10, 1942. All of the meetings and both the Commercial and Educational and Scientific Exhibits will be held in the Municipal Auditorium.

The various committees have been set up and the following Chairmen have been appointed:

Executive Committee	DR. FRED L. ADAIR, Chicago
Program Committee	DR. E. D. PLASS, Iowa City
Motion Picture Committee	DR. ROBERT D. MUSSEY, Rochester
Educational and Scientific Exhibits	DR. H. CLOSE HESSELTINE, Chicago
Commercial Exhibits	DR. PHILIP F. WILLIAMS, Philadelphia
Lay Publicity	DR. JOSEPH L. BAER, Chicago
Professional Publicity	DR. GEORGE W. KOSMAK, New York
Publications Committee	DR. GOODRICH C. SCHAUFFLER, Portland
Evening Meetings	DR. ROBERT L. DENORMANDIE, Boston
Membership Committee	DR. BUFORD G. HAMILTON, Kansas City
Budget and Finance Committee	DR. WILLIAM C. DANFORTH, Evanston

The general plan for the program will be much the same as that of the first Congress, which was held in Cleveland, Sept. 11 to 15, 1939, with sectional meetings for the various groups (nurses, public health, administrators, educators, and physicians), general sessions for all members attending the Congress and round tables. There will be evening sessions open to the general public.

Adequate time for registration will be given the first day, before the opening of the sessions of the Congress. Admission to the Congress will be by individual membership card only. These may be secured by payment of the five dollars registration fee, any time after Sept. 1, 1941.

At the suggestion of the Medical Exhibitors Association, more time will be allowed for the members of the Congress to visit the Exhibits. The response to a letter sent to the firms handling products of interest to our group telling them of a second Congress has been excellent and we are assured of an excellent Commercial Exhibit.

The hotel headquarters have not been assigned to the various groups as yet, but the Medical Section and General Congress Headquarters will be in the Jefferson Hotel.

For further information, apply to the Chicago office of the Congress, 650 Rush Street.

Erratum

In the article, "Jelly Contraceptives," by Dr. Irving F. Stein, which appeared in the May, 1941, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, p. 853, lines 21 and 22, it is stated that Stix has shown that the diaphragm and jelly method is only 76 per cent effective in relief recipients. This figure should be corrected to read 85 per cent.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. *President,* W. C. Danforth. *Secretary,* H. C. Taylor, Jr., 830 Park Ave., New York, N. Y. Next meeting, May, 1942, Sky Top, Pa.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. *President,* Frederick H. Falls, Chicago, Ill. *Secretary,* James R. Bloss, 418 11th Street, Huntington, W. Va. Annual meeting will be held at the Homestead, Hot Springs, Va., September 11 to 13, 1941.

Central Association of Obstetricians and Gynecologists. *President,* Thomas B. Sellers, New Orleans, La. *Secretary-Treasurer,* W. F. Mengert, Iowa City, Iowa. Next meeting, New Orleans, La., Fall of 1941.

South Atlantic Association of Obstetricians and Gynecologists. *President,* R. A. Bartholomew, Atlanta, Ga. *Secretary,* Robert A. Ross, Durham, N. C. Next meeting, February, 1942, Atlanta, Ga.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* W. T. Dannreuther. *Secretary,* Philip F. Williams, 2206 Locust St., Philadelphia, Pa. Next meeting, June, 1942, Atlantic City, N. J.

New York Obstetrical Society. *President,* H. J. Stander. *Secretary,* Ralph A. Hurd, 37 E. 64th Street, New York City. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. *President,* T. L. Montgomery. *Secretary,* John C. Hirst, 500 North 20th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. *President,* Harold K. Gibson. *Secretary,* James A. Gough, 104 S. Michigan Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. *President,* George G. Cochran. *Secretary,* John J. Madden, 362 Washington, Ave., Brooklyn N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Avenue, Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. *President,* Abraham Samuels, *Secretary-Treasurer,* Frank K. Morris, 11 East Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Building.

Cincinnati Obstetrical Society. *President,* E. W. Enz. *Secretary,* Edward Friedman, 19 West Seventh St., Cincinnati, O. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Robert F. Monroe. *Secretary,* Layman A. Gray, 332 West Broadway, Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Howard Stearns. *Secretary,* William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. *President,* S. A. Chalfant. *Secretary,* Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.

Obstetrical Society of Boston. *President,* John Rock. *Secretary,* Judson A. Smith, 264 Beacon St., Boston, Mass. Third Tuesday, October to March, Harvard Club.

New England Obstetrical and Gynecological Society. *President,* Frederick L. Good. *Secretary,* R. J. Heffernan, 475 Commonwealth Avenue, Boston, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. *President,* John Vruwink. *President-Elect,* T. Floyd Bell. *Secretary-Treasurer,* William Benbow Thompson, 6253 Hollywood Boulevard, Los Angeles, Calif. Next meeting, Los Angeles, Calif., November 5 to 8, 1941.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL.

Washington Gynecological Society. *President,* R. L. Sylvester. *Secretary,* W. R. Thomas, 1830 K. Street, N. W., Washington, D. C. Fourth Saturday, October to May.

New Orleans Obstetrical and Gynecological Society. *President,* E. L. Zander. *Secretary,* Eugene Countiss, 921 Canal St., New Orleans, La. Meetings held every other month.

St. Louis Gynecological Society. *President,* E. Lee Dorsett. *Secretary,* Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Second Thursday, October, December, February, and April.

San Francisco Gynecological Society. *President,* T. Henshaw Kelly. *Secretary,* R. Glenn Craig, 490 Post Street, San Francisco, Calif. Regular meetings held second Friday in month, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. *President,* Roy Grogan. *Secretary,* J. McIver, 714 Medical Arts Building, Dallas, Texas. Next meeting, Galveston, Texas, September, 1941.

Michigan Society of Obstetricians and Gynecologists (formerly the Detroit Obstetrical and Gynecological Society). *President,* Russell W. Alles. *Secretary,* Harold C. Mack, 955 Fischer Bldg., Detroit, Mich. Meeting first Tuesday of each month from October to May (inclusive).

Obstetric Society of Syracuse Hospitals. *President,* Francis R. Irving. *Secretary,* Nathan N. Cohen, 713 East Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. *President,* T. M. Boulware, Birmingham, Ala. *Secretary,* Eva F. Dodge, 519 Dexter Avenue, Montgomery, Ala. Next meeting, Mobile, Ala., April, 1941.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Texas. Meetings held first Tuesday of each month at Gunter Hotel.

Books Received

THE MASK OF SANITY. By Hervey Cleckley, professor of neuropsychiatry, University of Georgia School of Medicine. 1941. The C. V. Mosby Company, St. Louis.

ESSENTIALS OF GYNECOLOGY. By Leo Brady, assistant professor of gynecology, University of Maryland, etc., and Ethna Louise Kurtz, R.N., head nurse, Brady Urologic Institute, Johns Hopkins Hospital, etc. 57 illustrations, 251 pages. 1941. The Macmillan Co., New York.

WOLF CHILD AND HUMAN CHILD, being a narrative interpretation of the life history of Kamala, the wolf girl. By Arnold Gesell, M.D., director of Yale University Clinic of Child Development. Illustrated with photographs and drawings, 107 pages. 1941, Harper and Brothers, New York.

THE HEART IN PREGNANCY AND THE CHILDBEARING AGE. By Burton E. Hamilton, M.D., cardiologist to the Boston Lying-in Hospital, and K. Jefferson Thomson, M.D., associate physician, Metropolitan Life Insurance Company Sanatorium, etc. With a section: Delivery and Obstetrical After-Care of Cardiacs, by Frederick C. Irving, professor of obstetrics, Harvard Medical School, etc. 402 pages. 1941, Little, Brown and Company, Boston.

TEXTBOOK OF PEDIATRICS. By J. P. Crozer Griffith, emeritus professor of pediatrics in the University of Pennsylvania, etc., and A. Graeme Mitchell, professor of pediatrics, College of Medicine, University of Cincinnati, etc. Third edition, revised and reset, 220 illustrations, 991 pages. 1941. W. B. Saunders Company, Philadelphia.